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EDITORIALS

An Appraisal of Chemotherapy As an Adjuvant to Surgery for Cancer

THERE is increasing experimental evidence that chemotherapy, employed as an adjuvant to surgery for cancer, may lead to increased cure rates of neoplastic disease. The growing interest in this concept suggests that full appraisal may serve a useful function.

The frequent lack of success attending "resection for cure" is ascribed to the continued presence of neoplastic cells despite apparently complete removal. These residual malignant cells fall into the following categories: Category 1: cells already established ("rooted") at the time of surgery. These are distant metastases, the existence of which is not initially appreciated. Category 2: cells that are released into the circulation and/or lymphatics at the time of surgery. These possess the potential of becoming established and thereby result in metastases. Category 3: cells released into the operative area by direct seeding at the time of surgery. These also possess the potential of becoming established, and thereby result in local tumor implants.

To define accurately the place of chemotherapy as an adjuvant to the surgical treatment of cancer, the relative importance of these three categories in producing surgical failure must be assessed. Although insufficient information is available at present to allow precise quantitation of the role played by each of these three groups, enough data have been accumulated to permit comparison.

It has been documented by wound washings, examination of blood and local tumor recurrences at the suture line that cancer cells may be disseminated into the blood stream and into the wound by operation. This may suggest that the most significant factor responsible for surgical failure is the high percentage of seeding of cancer cells occurring during operations for malignant tumors. More discriminating evaluation, however, reveals that this implied cause-effect relationship is more apparent than real. Thoughtful study of the available data reveals that in most instances these "escaping" cells are destroyed before they can become established as metastases. These studies further suggest that heavy dissemination of cancer cells into the circulation must occur daily over the entire life span of a malignant growth. If the daily release of multitudes of cancer cells into the blood stream were to result very frequently in metastases, surgical cure rates would be virtually zero. It follows therefore that the presence of cancer cells in the blood stream does not necessarily, or often, imply an impending metastasis. In this regard it is pertinent to take cognizance of the laboratory data demonstrating that the implantation of a single cancer cell only rarely results in a tumor and that, generally, a certain size inoculum of cancer cells has been found necessary to initiate tumor growth consistently.

It would appear then that the presence of seedings of cancer cells is only infrequently associated with metastases. The wide discrepancy between these facts and the relatively high incidence of surgical failures that are observed, argues strongly that the major reason for surgical failure must lie in the existence of

established tumor cells at the time of surgery—the unsuspected metastases.

If the major cause for failure in surgery for cancer exists in the form of the missed metastasis, the greatest success in augmenting surgical cure rates by employing adjuvant chemotherapy can come only from agents capable of destroying residual *established* cancer cells. The discovery of such compounds is the major problem in the field of adjuvant chemotherapy. At this time, unfortunately, all those compounds shown capable of producing cure of early tumor transplants have been found markedly less effective (merely inhibitory) against the same type tumor transplants in a well established phase of growth. Recent experimental evidence [1] reveals that surgical excision of the bulk of such well established tumors renders a residual small tumor mass (still established) once again vulnerable to chemotherapeutic cure. These preliminary laboratory results suggest that surgical removal of all gross cancer tissue may render small metastatic lesions susceptible to appropriate chemotherapy. Thus it would appear that chemotherapy may serve a most useful function with surgery for cancer.

On the other hand, surgeons stand to make a substantial contribution to cancer chemotherapy. Removing the bulk of tumor tissue may provide, at a clinical level, the necessary conditions for optimal detection of appropriate and effective agents. Thus surgeons may be in the best position to find the agents that will prove most useful.

There is evidence to suggest that freely floating cancer cells are more vulnerable to chemotherapeutic attack (category 2) than established cells. It is well known that transplanted tumors are more susceptible to chemotherapy during the first few days after transplantation before they become established. On the same basis, it may be that freely floating cancer cells will be destroyed by systemic administration of only a small dose of a chemotherapeutic agent. There is experimental evidence demonstrating the effectiveness of nitrogen mustard analogues in destroying cancer cells before they become established, and clinical trial of certain of these alkylating agents as adjuvant therapy to surgery for cancer is currently under way. To place such studies in proper perspective, however, it is necessary to point out that agents limited in their carcinocidal power to non-established cancer cells can at best eliminate only an estimated small percentage of the total group of surgical failures.

A very small percentage of the total group of surgical failures would seem to be due to implantation of cancer cells into the local wound (category 3). It is within this category that adjuvant chemotherapy might be expected to be most readily successful. Since wounds may be washed with much higher concentrations of chemotherapeutic compounds than could safely be administered systemically, it should be easier to destroy residual, freshly sown cancer cells. However, any drug utilized for this purpose must necessarily be of limited value as an adjuvant to surgery for cancer, since apparently only a tiny percentage of surgical failure is due to local tumor implants. For this reason, proper clinical evaluation of this type of drug might be best accomplished by restricting clinical study to cancer types having reasonably high local recurrence rates undoubtedly due to implantation (e.g., anterior resections for rectal cancer) as opposed to lymphatic permeation.

Doubtless in the near future numerous agents will be judged potentially useful as adjuvant chemotherapy to the surgical treatment of cancer. Inasmuch as no correlation between laboratory tumors and human neoplasms has been demonstrated, clear translation of provocative experimental results into similarly successful clinical use is not predictable. This situation permits the possibility of inadequate evaluation of these potential agents. Aside from erroneously concluding that a compound is active, there is the greater danger that negative results may permit the abortive dismissal of adjuvant chemotherapy as a non-fruitful approach and lead to its abandonment. Thoughtful consideration of the experimental data associated with each candidate compound, keeping in mind the many complexities involved in the study of adjuvant chemotherapy, should lead to intelligent formulation of clinical studies with the attainment of meaningful answers in relation to the three general categories of target tumor cells outlined herein, and their relative importance.

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[1] SHAPIRO, D. M. and FUGMANN, R. A. A role for chemotherapy as an adjunct to surgery. *Cancer Res.*, 17: 1098, 1957.

On the Utilization of Medicomilitary History

THE title of this editorial is unblushingly derived from an interesting collection of addresses entitled "On the Utility of Medical History," which were presented before the Institute on Social and Historical Medicine held at the New York Academy of Medicine in 1957 [1].

As the Editor, Dr. Iago Galdston, stated in the introductory lecture, medical history has long been cultivated as an avocation by those with a bent for the humanities, but for practical purposes, the field is yet to be exploited as fully as it might be. The participants in this institute were therefore invited to consider whether the historical knowledge of medicine might be utilized to comprehend and resolve some of the problems with which medicine is now beset.

In the beginning, at least, some of the invited speakers did not view the idea of the utility of medical history with any particular degree of enthusiasm. The Editor, from the beginning, took a different point of view. Like Francis Bacon, who wrote that "Histories make men wise," Dr. Galdston concluded that the utility of medical history, as of history in general, "derives from the fact that [it] is that discipline which exposes and expounds the basis upon which judgment can best be founded." In short, it offers "the point of departure, from which one may set out on the adventure of judgment."

One of the wisest and most perceptive statements in this series of lectures was made by Gregory Zilboorg, to the effect that throughout the course of the history of medicine there runs not only the history of ideas but the history of the loss of ideas. Anyone who writes on the utilization of medicomilitary history might well take the history of the loss of ideas as his theme.

A military history, as Hanson W. Baldwin, Military Editor of the *New York Times*, has pointed out, demands not only funds for its production but, if it is to fulfill its real usefulness, readers for its text. Its utilization by those who should read it depends upon its distribution and upon the publicity which it receives. Baldwin's statements are equally applicable to medicomilitary history, as the past shows very clearly.

The medical history of the Civil War, almost a hundred years after its publication, still has much of value in it, but it never fulfilled its real usefulness. Its distribution was chiefly through Congress, which meant that it was chiefly on a private, individual basis. The volumes, for the most part, went into private libraries and they were thus not available to those who might have profited most by their perusal.

The distribution of the history of the U.S. Army Medical Department in World War I was wiser but it was still not satisfactory. Other circumstances also militated against its wider use. The first notice of the first published volume, in a medical journal of very wide circulation, described it as a "report" by the Surgeon General, a trivial error, it is true, but one explanation of why many potential readers, such as medical reserve officers no longer in service, remained in permanent ignorance of the existence of the World War I history. No formal attempt seems to have been made to publicize and utilize the volumes when thousands of medical officers entered the service from civilian life at the outbreak of World War II. Finally, these volumes, like the volumes of the Civil War history, were characterized by what the Editor of the World War I history, Brigadier General Frank W. Weed, described as "ponderosity." They do not lend themselves physically to ready use. Colonel (later Major General) Guy B. Denit, MC, is said to have gone ashore in North Africa carrying the surgical volumes of the World War I history as part of his essential impedimenta, but he was almost unique in both his physical stamina and his knowledge of their existence.

We paid dearly for this ignorance in World

[1] GALDSTON, I. Editor. On the Utility of Medical History. New York, 1957. International Universities Press, Inc. (Monograph 1, Institute on Social and Historical Medicine, The New York Academy of Medicine.)

War II. The last volume of the World War I history was published in 1929, and the work was well done. If the recorded experiences had been put to use at the outbreak of World War II, in which we found ourselves actively engaged only twelve years later, costly errors of omission and commission could easily have been avoided. Instead, the volumes remained on the library shelves then, as they had since their publication, and that, to quote another speaker in the New York Academy symposium, amounts to no more than "material preservation as a physical object."

The history of the U.S. Army Medical Department in World War II is part of a total series of about 125 (proposed) volumes dealing with all aspects of the war in all theaters of operations. About fifty of these volumes are being prepared and published under the direction of the Surgeon General.

The medical history, for a variety of reasons, got off to a very bad start. There were numerous changes of policies and plans, some of them basic. There were also changes of direction. The present incumbent, who assumed his duties in July 1954, is the fifth Editor-in-Chief, Finally, the publication of a series of books through medicomilitary channels is a far more complicated process than the accomplishment of the same feat in civilian life.

Only one volume of the history was published between the end of the war in 1945 and October 1955. Since then, the situation has vastly improved. Thirteen other volumes were published in the 1955–1958 period; seven others are in press or being processed for the printer and all but six of the total number planned are now in various stages of preparation. Of the fourteen volumes published to date, eight are in the surgical series, and the volume on cold injury, in the miscellaneous series, contains much of interest to surgeons. There will be at least six more volumes in the surgical series, one of which, the second neurosurgical volume, is now ready for press.

The fate of previous medicomilitary histories must not be allowed to befall the history of the U.S. Army Medical Department in World War II. We are making earnest efforts to see that it does not. The distribution has been carefully planned. A letter from the Surgeon General, calling attention to the purpose of the historical project and to special points of interest in the volume presently being distributed, goes out with each volume to medical school libraries, Army installations, medical journals which receive copies for review, individuals in governmental agencies, medical services in other countries, and members of Congress who request copies.

A Promotion Branch in the Historical Unit, U.S. Army Medical Service, handles publicizing of the history, including the preparation and circulation of informational material and the preparation and demonstration of exhibits at general and special medical meetings. There has been a remarkable display of interest in these exhibits and a distressing lack of any previous knowledge of the existence, let alone the scope, of this history.

The preparation of the volumes already published and of those in preparation is in the sound historical tradition. There has been no attempt to gloss over errors, a point upon which a number of reviewers have commented favorably. The lessons of the past must be utilized for the future, and this cannot be done unless there is a frank confession of mistakes.

The series comprises both clinical and administrative volumes but pertinent administrative details are also presented in every volume of the clinical series. This is another point upon which reviewers have commented favorably. Quite evidently they understand that without a sound logistic system, the best clinical skill in the world cannot be used to maximum effectiveness.

The surgical volumes, like the other volumes of the history, are of real practical value. Young men now in medical school must, most of them, be prepared to serve in the Medical Corps of some one of the Armed Services when they complete their training. Their service will be easier and more profitable for them if they enter upon it with the knowledge set forth in these books.

Instructors in the MEND (Medical Education for National Defense) program will find these volumes of great usefulness in their work, particularly when the material in them is supplemented by the material in "Emergency War Surgery," the modification of the NATO handbook on the same subject just published for the use of all our Armed Forces [2]. Surgeons

[2] Emergency War Surgery. NATO Handbook. U.S. Armed Forces issue of NATO Handbook prepared for use by the Medical Services of NATO Nations. United States Department of Defense. Washington, D.C., 1958. United States Government Printing Office.

in civilian practice will find the clinical material on trauma of great value.

Finally, these volumes can be of inestimable use in the preparation for the war that may never come but for which, in the present state of the world, we must be constantly prepared. Ignorance in problems that arise out of war or other mass catastrophe has a very high cost. The ability to care for large numbers of seriously wounded persons must be part of the armamentarium of all physicians in this mechanized and thermonuclear age.

The reception of the volumes of the history already published bears out what has just been said about their potential usefulness. Reviews have, on the whole, been favorable as well as fair. We have deserved the few adverse criticisms we have received; they chiefly concern the delay in publication, upon which a comment has already been made.

It is significant that the majority of reviewers stress the tragic fact that the lessons of World War I, so clearly set forth in the medical history of that conflict, had to be learned over again, at high cost of life and limb, in World War II. They are therefore insistent that these volumes must be read and digested to forestall a similar tragedy if another war comes, and their remarks cannot be ignored in the present state of the world.

The publicity given to these volumes by reviews in many journals and by special displays in medical libraries has been a real contribution to the national defense. The chief reason for the deliberate effort to publicize this project is not, of course, to sell books (although it might be said that the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C., has them for sale at remarkably low prices). The purpose is, instead, to make sure that the old aphorism does not again come to pass, as it has in so many previous wars, that the lesson of history is that the lesson of history is never learned.

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Vulvectomy

A REVIEW OF FIFTY-FIVE CASES

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VULVECTOMY is a relatively uncommon operation and seldom does one surgeon have the opportunity to gain enough personal experience with this operation and the lesions involved. For this reason, the vulvectomies performed at the Ohio State University Hospital from 1942 through May 1957 are herein reviewed. It is hoped that from this study we may learn more about the surgical aspect of vulvar disease.

MATERIAL

The cases selected consist of all the vulvectomies performed during the previously stated fifteen-year period. For the purposes of this selection, vulvectomy was loosely defined as the surgical excision of a circumferential portion of the vulva. Those cases in which lesions of the vulva were locally excised were eliminated. Within this loose definition, the extent of vulvectomy varied from the simplest excision of the labia minora and inner aspect of the labia majora to wide vulvectomy and bilateral Bassett type inguinal node dissection.

Fifty-five vulvectomies make up the material studied. Of these, twenty-eight were performed for malignant vulvar lesions and twenty-seven for benign conditions. These two groups will subsequently be referred to as the malignant group and the benign group. Thirty of these patients were private patients of the attending staff. Of these, thirteen were in the malignant group and seventeen in the benign group. The remaining twenty-five patients were on the teaching gynecology service and of these, fifteen were in the malignant group and ten were in the benign group.

DISTRIBUTION ACCORDING TO AGE

The average age of the patients in the malignant group was 59.0 years. This figure is gratifying because it corresponds exactly to the average age in a larger group reported by Taussig [1] and may lend support to the statistical significance of this small series. Carcinoma of the vulva is characteristically a disease of elderly women [2]. However, in this series there were five patients below the age of forty. Further breakdown of the age distribution is seen in Table 1.

The average age of the patients in the benign group was 58.0 years and the patients are rather evenly distributed from the ages of forty through eighty years as indicated in Table 1.

RACIAL DISTRIBUTION

In this series there were fifty-two white and three Negro patients. This figure is remarkable in that the percentage of Negroes for all admissions to this hospital is approximately 18 per cent and for the clinical services is approximately 40 per cent. Little mention is made in the literature concerning the racial incidence of vulvar lesions; however, it would seem safe to infer from this series that vulvar disease, both benign and malignant, excluding veneral lesions, is less common in Negro women. Perhaps the lack of Negroes in this series accounts for the fact that there are no so-called "post-

TABLE I
DISTRIBUTION OF PATIENTS ACCORDING TO AGE AND LESION

Age (yr.)	Benign Lesions* (No. of Cases)	Malignant Lesions† (No. of Cases)
20–29	0	0
30–39	2	5
40–49	4	3
50–59	8	6
60–69	7	6
70–79	5	7
80–89	1	1

* Average age of patients 58.0 years.
† Average age of patients 59.0 years.

TABLE II
PRESENTING SYMPTOMS

Primary Presenting Symptoms	No. of Cases
Benign lesions:	
Pruritus vulvae	23
Pain in perineum	1
Dysuria	1
Burning and swelling of labia	1
Painful lesion	1
Malignant lesions:	
Sensation of a mass or growth	10
Pruritus vulvae	7
Pruritic nodule or lesion	6
Ulcerated lesion	3
Pain in perineum	1
Burning excoriation	1

granulomatous carcinomas" of the vulva in our group. This is in marked contrast to the recent report from Johns Hopkins Hospital [3] of thirteen of fifty cases of vulvar carcinoma with pre-existing veneral granulomas and thirteen of ninety-three cases in the series reported from New Orleans [6].

Of the three patients in the Negro group, two had carcinoma and one had leukoplakia. Taussig [8] states that the atrophic vulvar lesions, including carcinoma, are extremely rare in the Negro race, whereas the hypertrophic forms of vulvitis with ulceration are almost entirely limited to it. He is referring specifically to vitiligo, kraurosis and leukoplakia and includes carcinoma in this subgroup of atrophic lesions.

SYMPTOMATOLOGY

Vulvar pruritus is the most common symptom in both the benign and the malignant groups. The frequency of pruritus in the patient with carcinoma is probably due to the frequently (approximately 50 per cent [1,4]) pre-existing leukoplakia of the vulva. In the benign group, pruritus is nearly always the presenting symptom whereas in the malignant group a significant number of patients will have noticed a "lump" or "sore" when they first report for examination. Table II outlines the presenting symptoms in the present series.

Saltzstein, Woodruff and Novak [3] comment on the unusual frequency of patient delay in cases of vulvar lesions which are on an exposed and easily examined area of the body. In our series, this was also noted and patients in both the benign and the malignant groups had many years of distressing pruritus while treating themselves or being treated unsuccessfully with ointment, lotions and all too frequently low dosage x-ray therapy. Seven patients of twenty-eight in the malignant group came to us with a history of receiving x-ray therapy which was in each case totally inadequate and only contributed to the medical delay in the proper treatment. Most authorities have agreed that the treatment of choice for the often highly differentiated epidermoid carcinomas of the vulva is surgery [2,4,5,8]. X-ray treatment is indicated only in extremely poor risk patients or for palliation of far advanced cases. Two patients in the benign group had ineffective x-ray therapy prior to vulvectomy. Taussig [8] believes that x-ray treatment of leukoplakia is only indicated in the surgically poor risk patient.

The average duration of symptoms in the malignant group prior to admission for vulvectomy was 2.68 years with a range of two weeks to fifteen years. For the benign group, the average duration of symptoms was five years with a range from two months to twenty-five years.

ASSOCIATED AND CONTRIBUTORY FACTORS

In any study of vulvar lesions one may frequently encounter several associated conditions which because of their frequency must be considered contributory to vulvar disease. These conditions are: (1) age, (2) diabetes mellitus, (3) obesity and (4) psychoneurosis.

It has been previously noted that vulvar lesions are most common in elderly women aver-

aging fifty-eight and fifty-nine years of age, respectively, for benign and malignant groups in this series. For this reason there is presumed a causal relationship between vulvar lesions and estrogen deficiency [4,7] and many researchers have reported success with topical estrogen treatment of kraurosis, in particular.

Diabetes mellitus occurred six times in this series of fifty-five cases (10.9 per cent). There were three diabetics in each group (benign and malignant). Of these, two had leukoplakia (which underwent malignant change in one case), two had primary epidermoid carcinomas, one had kraurosis and one had "idiopathic" pruritus vulvae. The frequency of vulvar pruritus as a symptom of diabetes is well recognized [3] but little mention is made of its association with leukoplakia and carcinoma of the vulva. From this small series its associated incidence seems more than coincidental. In any event it is well to keep it in mind when examining a patient with a vulvar lesion.

Obesity sufficiently noteworthy to be recorded as part of the discharge diagnosis of the patient occurred four times in this series. No attempt has been made to correlate this with the general incidence of obesity in elderly women. It has, however, been pointed out frequently that chronic irritation is a factor in the production of epidermoid carcinomas and certainly a factor in the production of pruritus vulvae [9]. This irritation must certainly be common in the obese patient.

Overt psychoneurosis was recorded in three patients in this series. Two of these underwent vulvectomy for persistent pruritus vulvae and the pathologist reported only chronic inflammation in the submitted specimen. The remaining patient had a squamous cell carcinoma of the labia. In patients in whom neurosis coexists with pruritus vulvae it is difficult to know which came first. Certainly, pruritus seems to be a rather common symptom of the neurotic [9] but it is not difficult to imagine that the reverse might easily be manifest particularly in long-standing cases [2]. Case reports of suicide as an escape from the intractable itching have been reported [8].

MALIGNANT GROUP

Etiology. In contrast to the previously mentioned associated and predisposing conditions there are certain lesions that seem to bear a direct etiologic relationship to carcinoma of the vulva. Taussig [1] has enumerated the following in the order of their frequency as etiological factors: leukoplakia, syphilitic or postsyphilitic ulcer, senile warts, Bartholin's abscess, urethral caruncle and trauma. In ninety-seven of his series of vulvar carcinomas, one of these etiologic factors was involved. From these impressive figures he speculates that the incidence of vulvar carcinoma might be cut in half if these lesions were promptly and carefully treated.

In this series, from available records, only six of twenty-eight patients with carcinoma had pre-existing leukoplakia. One patient had a positive serology; none had pre-existing warts that were recorded as significant and none had recorded disease of Bartholin's glands, nor were any cases recorded as arising from urethral caruncles. One case is interesting in that a complete vulvectomy was performed for leukoplakia and at that time a urethral caruncle was noted. Subsequently, a periurethral carcinoma developed and more extensive vulvectomy with excision of the distal third of the urethra was carried out at another hospital. This probably represents a malignancy developing in a caruncle. This patient was sixty-one years of age.

Pathology. All twenty-eight patients in this group had squamous cell carcinomas, one of which was carcinoma *in situ*. Thirteen of these patients had complete bilateral node dissections performed and of these four were found to have positive nodes on pathological examination.

Seven patients showed no residual carcinoma in the vulvectomy specimen following excisional biopsy.

In our series the clinical or pathological diagnosis of carcinoma of the clitoris was made twice. This is a rare entity and when diagnosed is probably most often a secondary involvement of the clitoris by a primary lesion of the prepuce [1].

Included in the malignant group is one *in situ* carcinoma of the vulva or intraepithelial carcinoma. On the biopsy report this was designated as Bowen's disease which is incorrect and points up the frequently overlooked distinction between the two lesions as defined by Novak [10,11].

Operations Performed. Each patient in this group underwent complete vulvectomy. In addition, thirteen patients had bilateral complete Basset node dissections performed; colos-

tomy and excision of the anus and lower rectum for a lesion of the perineal body invading these structures were performed for one patient.

The choice of surgical procedure was based on several factors. Foremost was age and its relation to operative risk. The average age of the group of patients who did not have node dissections was seventy-one years as compared to fifty years for those who did. A total of ten patients were considered too poor a risk for node dissections. In addition to being poor risks, four of these had small lesions and one had a far advanced lesion. One other patient had a lesion too far advanced for node dissection and vulvectomy was performed only for palliation. Vulvectomy only was performed in the patient with carcinoma *in situ*. It is not known why the remaining two patients had no node dissection performed.

In six patients node dissection was carried out as a second stage procedure following vulvectomy by approximately ten days. This was performed in relatively poor risk patients to minimize the anesthesia and operating time at one sitting. This is somewhat less than ideal surgery for cancer but acceptable when indicated [*1,4*]. The presence or absence of palpable nodes is of value for clinical staging but should not influence the choice of surgery. Taussig [*1*] reports 21 and 42 per cent positive nodes in the surgical specimens for clinical groups I and II respectively. He, therefore, recommends the node dissection in groups I to III patients under sixty-five years of age and in early lesions of good surgical risk patients above this age. This age division is based on the sharp rise in operative mortality above age sixty-five.

Postoperative complications: There were no operative mortalities. Most noteworthy of the complications encountered was the failure of primary healing in the inguinal wounds of all but one patient having lymph node dissections. Wound separation, skin slough, fluid accumulation, hematomas and wound infections were seen in varying degrees of severity in all of these patients often prolonging hospitalization considerably. This is apparently not unusual in this series for it is commented on by both Taussig [*8*] and Te Linde [*4*] and adequate wound drainage, pressure dressings and dry heat applied to the wound postoperatively are recommended to minimize these wound complications. Primary grafting of vulvar wounds or the use of large sliding pedicles from the inner thighs have not been used in this series. There have been no serious sequelae from these wound complications and perhaps the risk of excessive scarring and prolonged healing is justified by the five-year survival statistics in most series of patients with vulvar carcinoma treated by vulvectomy and node dissection.

One other complication of the node dissection that deserves mention is the lymphedema of the lower extremities that follows interruption of the lymph drainage. This occurred in three cases of our series and was not considered of great importance by the patient.

Follow-up Data. Of the twenty-eight patients in this group, eighteen are living at the time of this report. All the remaining ten patients died as a result of carcinoma except one who died of intercurrent disease at the age of eighty-seven. Of the eighteen who are living, seventeen have no evidence of disease at this time. This yields an absolute survival rate from carcinoma of the vulva, postvulvectomy, of 68 per cent.

Of the nine patients followed up for five years or more, four had survived for an incidence of 44 per cent. This, of course, is an incidence in patients who underwent surgery since only patients who had undergone vulvectomy are included in this series. Of these nine patients operated upon prior to May 1952, only two underwent bilateral node dissections. One is living and one died from recurrent carcinoma. For comparison and review of five-year survival rates, we include several of the larger series reported. Collins, Collins, Nelson, Lewis and Cassidy [*12*] recently reported their follow-up of fifty-four consecutive cases of vulvar malignancies from Tulane University. In twenty-eight of these, vulvectomy plus bilateral node dissections were carried out. Twenty-six of their patients are eligible for five-year follow-up and they report 65 per cent living five years. In the group who underwent operation they have 74 per cent living five years. Included in their series were seven cases of intraepithelial carcinoma. Taussig [*17*] reporting on 101 cases of invasive carcinoma had an over-all five-year survival of 32 per cent and a 58 per cent five-year survival for those forty-one patients who underwent vulvectomy and Basset operations. Incidentally, he reports the remarkable 52.6 per cent five-year survival in the nineteen patients of his Basset group who had positive nodes histologically. This certainly should con-

TABLE III
PATHOLOGISTS' REPORT FOR BENIGN GROUP

Histological Diagnosis	No. of Cases
Kraurosis	11
Leukoplakia	10
Kraurosis and leukoplakia	2
Chronic inflammation of skin of vulva	2
Hyperkeratosis and chronic inflammation of vulva	1
Skin and subcutaneous tissue	1

vince the doubters of the value of lymph node dissection.

One of the three patients eligible for ten-year survival study in our series is living. None of the three patients had node dissections. Taussig [*1*] reports a 41 per cent ten-year survival in twenty-four of his patients treated by vulvectomy and Basset operations. There were four recurrences after five years.

BENIGN GROUP

Pathology. The pathologists' histological diagnoses for the benign lesions are shown in Table III.

In reviewing the literature for the preparation of this paper the condition of lichen sclerosus et atrophicus was frequently encountered. It is conspicuously absent from this list of pathological diagnoses.

Why is this lesion recognized by the dermatologist but ignored by the gynecologist and surgical pathologist? This proved to be a difficult question to answer.

Montgomery [*13*], who is given credit for establishing lichen sclerosus et atrophicus as an entity, in the conclusion of his (and Hill's) study refers to differential diagnosis of lichen sclerosus and kraurosis* and ponders why "these dissimilar conditions should have a similar histologic picture." They report lichen sclerosus to be six times as frequent in women as in men, unrelated to menopause, more frequently associated with lesions elsewhere on the body (in six of forty-six cases lesions were limited to the vulva, which was involved in twenty-six of the forty-six cases), and only occasionally pruritic. They suggest that in patients with intense itching there may be associated kraurosis or leukoplakia.

Allen [*14*] also believes that lichen sclerosus is a distinct entity and states that it can be clinically differentiated from leukoplakia and kraurosis chiefly by the follicular plugging and extension beyond the labia onto the thighs. He outlines its histologic characteristics and points out that lichen sclerosus et atrophicus is not premalignant but is characterized by exacerbations and remissions, is only mildly pruritic, and occurs commonly on the neck, shoulders, axillas, forearms and vulva.

Speiser [*7*] also refers to lichen sclerosus et atrophicus as a distinct entity and he believes that gynecologists have ignored this condition and mistaken it for the atrophic form of leukoplakia. He describes the whitish papules which are often confluent on the vulva forming symmetrical plaques. He points out that follicular plugging is difficult to observe in vulvar lesions. Histologic differentiation from leukoplakia is easily established according to Speiser but differentiation from well advanced kraurosis is difficult and the "two diseases may possibly be one and the same." It is suggested because of reports of carcinoma arising in lichen sclerosus et atrophicus, that frequent biopsies be performed to determine the presence of premalignant leukoplakia. He recommends no specific treatment, although he believes that topically applied cortisone may prevent progression if used early.

A case was presented by Boardman [*15*] in which a lesion with the typical distribution of lichen sclerosus et atrophicus was diagnosed as kraurosis by the pathologist following vulvectomy. This patient had had intense itching which was relieved by vulvectomy. The consensus of the group discussing the case was that histologically, differentiation from kraurosis was difficult, but that clinically, the absence of itching and the presence of lesions elsewhere on the body lead one to the diagnosis of lichen sclerosus et atrophicus.

Hunt [*16*] uses lichen sclerosus et atrophicus and leukoplakic vulvitis synonomously and thinks these lesions are definitely premalignant.

Many who discuss the differential diagnosis believe that leukoplakia does not extend beyond the inner aspect of the labia majora. Just as many authors [*2,8,17*], however, describe

* Montgomery and Hill, and Allen use the term kraurosis interchangeably with the atrophic stage of leukoplakia. This creates considerable confusion in the literature and is quite prevalent among the earlier authors. We prefer to distinguish kraurosis as pure, simple atrophy as proposed by Novak [*1*].

leukoplakic lesions perianally and laterally in the characteristic pattern ascribed to lichen sclerosus et atrophicus by its proponents.

The confusion is obvious and until someone can establish satisfactory diagnostic criteria, the gynecologist will continue to call these lesions leukoplakia and treat them by vulvectomy while the dermatologist will call them lichen sclerosus et atrophicus and treat them less vigorously.

Operation and Complications. The operation performed for the patients with benign lesions in this report were all simple vulvectomies by virtue of their inclusion herein. Two of these patients had anterior vaginal plastic procedures carried out at the same time.

Postoperative complications in this group were minimal. Five patients had minor wound separations and one patient had a severe wound separation requiring débridement and secondary closure. There was no operative mortality.

Follow-up Data. For eighteen of the twenty-seven patients in this group, adequate follow-up data are available. Many of the others who were seen only once postoperatively are presumed to be asymptomatic, but cannot be reported upon on the basis of a single visit four to six weeks postoperatively. Of the eighteen patients who were followed up for a period of at least six months, seven had recurrences of their preoperative symptoms; vaginal stenosis occurred in five; and a urethral carcinoma developed in one and has been mentioned previously. There was one pregnancy following vulvectomy which ended in spontaneous abortion at three months for reasons probably not related to the vulvectomy. Few patients of this series were in the child-bearing age.

It should be noted that many of the recurrences were minor and readily controlled by symptomatic treatment. In most of these cases, the surgeon was satisfied with the result of vulvectomy. Several of the vaginal stenoses were easily corrected by subsequent surgical procedures.

SUMMARY

Fifty-five cases of vulvectomy are reviewed with comments upon the pathologic conditions, surgical indications and complications encountered. Follow-up data are included for both the benign and the malignant lesions.

A brief review of the literature and a discussion of lichen sclerosus et atrophicus emphasize the controversial aspects of its diagnosis and treatment.

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Muscle Adenylic Acid As an Adjunct to Prepare Patients with Phlebitis and Ulcers for Definitive Surgery

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MUSCLE adenylic acid or adenosine-5-monophosphate is found quite generally in the red blood cells and platelets of the body. There is an accumulation of its concentration effects in various parts of the system. The reduction or elimination of this substance in some parts of the body apparently interferes with concentration of fluid volume in those cells so affected.

Rottino [1], in utilizing this substance as a trial method to reduce some of the weaknesses and fatigue of Hodgkins' disease, noticed that the pruritus which occurred so often in this disease as it advanced in intensity was relieved.

As a result of this finding, we made a careful test of the effects of this substance* on patients with varicose and phlebitic veins and ulcers in the Vascular Clinic at St. Vincent's Hospital. This work was reported first in 1950 [2], again in 1952 [3], and in 1954 [4].

The present report has to do with conclusions drawn from a review of this work and additional study in our Vascular Clinic.

The substance was administered to over 150 patients, to others by intramuscular injection, to some by rectal suppository and to a third group as pills by mouth. Thirty-six patients who could be carefully followed up were selected for study and the results are thus reported. Twenty of these patients were treated by the rectal suppository method and the rest were given intramuscular injections. It was determined early that the oral method of treatment was not effective.

* Called My-B-Den,® product of the Ames Co., Inc., Elkhart, Indiana.

Number and Type of Patients. Twenty of these patients were men and sixteen were women. The average age of the men was seventy-two and the average age of the women was sixty-seven. The duration of treatment varied from three weeks to four years. Twelve of these patients had no other type of therapy and twenty-four had supportive measures with or without active treatment of attendant infections. Note: At no time has one method of therapy been followed exclusively if it was believed that a substitute or additional one would improve the patient's condition.

Methods of Administration. Oral administration of this substance was ineffective except in four patients who appeared to be aided as much by their soaks and supportive methods as by the pills. Substitution of another type of pill was used as a placebo and these four patients improved. The rectal suppositories were usually given in the strength of 100 mg. three to five times a week. Suppositories are much easier to order and control in a clinic than are the intramuscular injections. When the injections were used, 100 mg. were injected three times a week.

Results of This Treatment. In six of twelve patients the use of My-B-Den alone caused no appreciable improvement in their status. In the other six patients it caused marked clinical improvement. In twenty-four patients the use of My-B-Den in addition to some type of physical supportive therapy or elimination of infection by antibiotics caused quite prompt healing of the ulcers. Eight of these patients had recurrence promptly after the treatment was discontinued. All eight of these patients' ulcers healed again when the adenylic acid therapy was resumed.

Infection. For any of the varicose or phlebitic ulcers that appeared to be locally infected, cultures and sensitivity tests were run and the correct antibiotics for the predominant organism were given in addition to My-B-Den therapy. In most instances (65 per cent) penicillin was given by injection, 300,000 μ intramuscularly three times a week. As soon as the infectious part of the process had been controlled by antibiotics, the My-B-Den was then used alone. This combination of methods was effective in twenty of the twenty-four patients.

Subsequent Therapy. In all patients who had varicose ulcers, after healing was effected or there was no longer evidence of inflammation the underlying diseased veins were resected and stripped. In the phlebitic type of ulcer, where there were adequate deep veins as shown by a venogram, the incompetent superficial and perforating veins were resected and stripped with excision of the areas of chronic thrombosis. Occasionally in patients with pruritus some dermatitis developed even after such subsequent surgery. In all but two instances the resumption of My-B-Den was effective in clearing the pruritus and the dermatitis.

Anticoagulant Therapy. If there were any signs of thrombophlebitis, the patient was actively treated with anticoagulant therapy in addition to other treatment.

Method of Action. The method of action of this substance is not clear. In a number of cases biopsy specimens were taken before and after administration of the drug. In each of these cases in which the drug was given by the suppository or intramuscular injection method, the concentration of the muscle adenylic acid accumulated in the biopsy tissue when tested enzymatically, and the edema seen in the biopsied epithelium of the cells before therapy was decreased. Epithelization of the ulcer was noted to increase microscopically.

This method of testing the ulcer microscopically before and after treatment was not practical. Patients might permit biopsies of an open ulcer but they would not cooperate to permit a biopsy when that ulcer was healed, due to fear of a new ulcer.

These enzymatic and pathologic methods to test the action of muscle adenylic acid on the ulcer specimens were done before and after the treatment. At the same time a second specimen was submitted for enzymatic determination of the qualitative content of the adenosine in the cell fluid. A definite correlation between the concentration of the adenosine and the dosage, however, seemed clear.

CONCLUSIONS

Muscle adenylic acid is an excellent additive to therapy for the preparation of patients with phlebitic and varicose ulcers with dermatitis. It is of value especially to those with pruritus. This is true provided that any infection is successfully treated by antibiotics and soaks. The substance is not effective in cases of infection by itself. It does shorten the time of preparation for definitive vascular surgery. At no time should the use of this substance be considered as a substitute for eventual surgical therapy for the underlying venous disease. It should be pointed out that sometimes patients get such good results from the injections of adenosine that they wish no other type of therapy and they will return for My-B-Den injections indefinitely. For that reason this substance should be used only for preliminary preparation. When carried out with supportive therapy and removal of infection it is an excellent correlative substance in preparing patients for operation. Certain failures would occur, and we could never be certain whether these were due to the ineffectiveness of the substance or lack of cooperation by the patient. There has been only one case of apparent allergic reaction. In this case a rash developed which was not unlike that of a mild reaction to penicillin.

If muscle adenylic acid is used as an adjunct and not as definitive treatment, the substance reduces the preparatory time for patients with ulcers prior to their surgical correction. This final operative treatment requires: (1) venograms in the patient with phlebitis to be certain the deep veins are functioning; (2) complete excision of the diseased veins; (3) in most cases wide excision of the ulcers and skin grafts.

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Bilateral Mixed Tumors of the Parotid Gland

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Bilateral mixed tumors of the parotid salivary glands are rare, only nine such cases being on record* [1,2,3,5,13,14,18,24,30]. The tenth case is reported in this paper.

Brown, McDowell and Fryer in 1950 reported one case in a series of 115 patients with mixed tumors of the parotid salivary gland [5]. Hoffman reported a case with an interesting history of bilateral epidemic parotitis approximately thirteen years previous to the development of bilateral mixed tumor [18]. Boley and Robinson, from a series of 103 cases of salivary gland tumors at the University of Kansas Medical Center, reported one case of bilateral mixed tumor [3]. They also reported two other cases of bilateral parotid tumors, one a Warthin's tumor and the other a parotid adenoma.

In 1954 the experience at the Memorial Hospital for Cancer and Allied Diseases in New York City was summarized from a series of 877 cases of parotid tumors; no case of bilateral mixed tumor was reported. However, in this report Frazell [14] cited a case of Wuester which had three typical benign mixed tumors, two of which were situated in the right parotid and the other in the left parotid gland. Also mentioned was Slaughter's case of a primary multiple mixed tumor, one in the right parotid gland and the other in the homolateral submaxillary gland.

In order to ascertain further the rarity of bilateral involvement of the major salivary gland with mixed tumor, inquiries were sent to various leading medical centers. Although the questionnaires which were sent requested rather particularized data, few of the answering institutions complied fully with our request. This is not an unusual observation. Nonetheless, approximately 50 per cent of the institutions acknowledged the questionnaires and made some effort to answer the questions submitted, if not entirely, at least in part.

The Los Angeles County Hospital (10,000 tumors are numbered in their registry) found no cases of bilateral tumors of the parotid gland [4]. Ellis Fischel State Cancer Hospital, in a survey of their 22,000 general tumor cases, found no instance of bilateral mixed tumor of the parotid salivary gland [31]. George Washington University Hospital, with an admission of 17,000 general cases annually, has no case of bilateral mixed tumor of the parotid gland on record [28].

In answer to our questionnaire the University Hospital of Wisconsin [21], Massachusetts General Hospital [8], M. D. Anderson Tumor Institute in Texas [32]. Ancker Hospital in St. Paul, Minnesota [27], Ohio State University Hospital [36], University of Oregon Medical Center [20], Henry Ford Hospital [19], Indiana Medical Center [35], University of Chicago Clinics [38] and the University Hospital in Ann Arbor, Michigan [15] all reported no cases of bilateral mixed tumor. Among the other institutions responding to the questionnaire, no new cases were reported [9–12,16,17,22,23,25,29,33,34,39].

At the American Oncologic Hospital only one case of bilateral mixed tumor was found in 16,000 admissions.

CASE REPORT

I. R., a thirty year old white woman, was first seen in the private office of one of us (S. G. C.) on March 5, 1954, with a mass in the right parotid area.

* Based on a survey of the literature from 1930 to 1957.

FIG. 1. Postoperative appearance after subtotal enucleation of the mixed tumor in the right parotid gland which was done elsewhere.

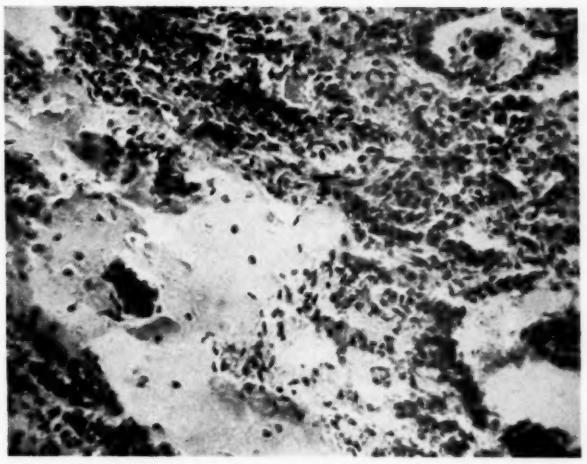

FIG. 2. Photomicrograph of the specimen removed from the right parotid gland which was diagnosed elsewhere as "adenocarcinoma." Correct diagnosis is mixed tumor.

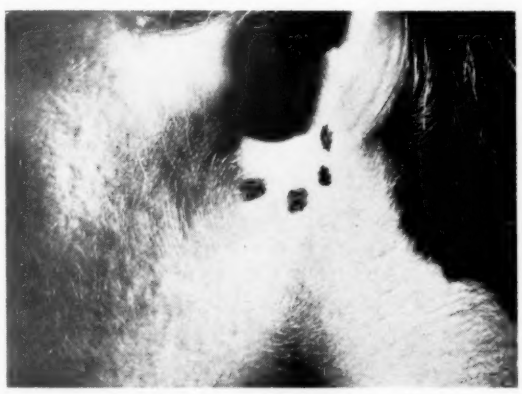

FIG. 3. Preoperative appearance of parotid area demonstrating the swelling produced by the mixed tumor in the left parotid gland. The ink dots outline the tumor mass.

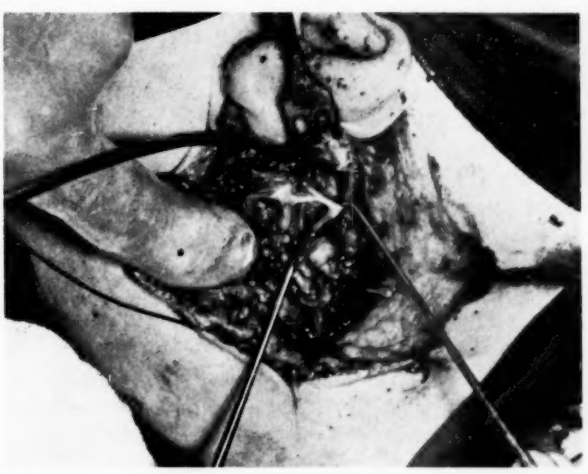

FIG. 4. Appearance at operation showing the main trunk of the left facial nerve and its principal branches. The main trunk should always be exposed at its point of emergence from the stylomastoid foramen in doing this type of surgical procedure.

Two years prior to consultation the patient had noted a lump in the area of the right parotid gland. She consulted a physician who advised her that she had a "cyst" and that it should be removed only if it caused distress. The patient did not seek further medical opinion but observed the mass for two years. During this time the tumor gradually increased in size and later became painful. Because of the pain the patient consulted an osteopathic physician who advised surgical removal of the tumor. The tumor was "excised" in an osteopathic institution and the lesion was reported to be an "adenocarcinoma of the parotid gland." She was then referred to the senior author for further treatment.

Past history revealed that in 1944 a mass had been excised from the same region as the present tumor. No additional information could be obtained to clarify this aspect of the patient's history. There was no familial history of neoplasia.

Examination at the time the patient was first seen revealed a swelling in the right parotid gland. A recent vertically placed, partially healed surgical wound, 5.5 cm. in maximum length, was present. The skin edges were approximated by six interrupted black silk sutures (Fig. 1) which were still *in situ*. Deep to the wound a palpable induration presented which measured about 3 by 7 cm. No nodes or satellite masses could be palpated in the neck. There was no evidence of facial paresis.

Routine laboratory examinations were within normal limits. A review of the histopathology in our own Department of Pathology led to the diagnosis of mixed tumor of the parotid salivary gland rather than "adenocarcinoma" as diagnosed elsewhere. (Fig. 2.)

FIG. 5. Specimen removed from the left parotid gland.

In view of the histopathologic findings, history of recurrence ten years later and evident incomplete removal of the tumor by morcellation, and the delay in receiving the slides and the tissue block for histopathologic confirmation, fractionated x-ray therapy was given. A total dose of 4,272 r was delivered to the surface of the skin and a total dose of approximately 6,000 r was delivered to the bed of the tumor.

Two years after completion of this treatment a hard mass, 2.2 cm. in diameter, was found in the left parotid area during routine follow-up examination. (Fig. 3.) The patient was advised of the importance of surgical removal of the tumor but she deferred until four months later. During this period the mass increased slightly in size. On September 20, 1956, subtotal parotidectomy was performed. (Figs. 4 to 7.) The histopathological report was "mixed tumor of the salivary gland (parotid)." To date there has been no evidence of recurrence of mixed tumor on either the right or left side.

FIG. 7. Postoperative appearance after subtotal left parotidectomy. No paralysis is observed as may be seen when the trunk or one of the main branches of the facial nerve is injured during surgery.

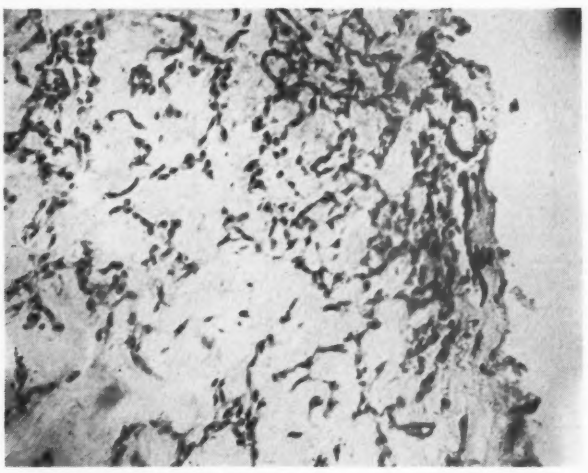

FIG. 6. Photomicrograph of the specimen removed from the left side. There is predominance of mucoid material when compared to that removed from the right side which has more epithelial elements.

COMMENTS

Bilateral mixed tumors of the parotid salivary gland are indeed rare. The case herein reported represents the tenth instance of bilateral mixed tumor of the parotid gland. A survey of the medical literature from 1930 to 1957 disclosed no additional cases to add to those reported and cited severally by different authors. A questionnaire directed to many leading American medical institutions disclosed no additional cases.

Even in a brief case report the original method of management of our patient demands comment. There are still surgeons who remove tumors of the parotid salivary gland by simple enucleation, even morcellation. Either method is to be condemned. Confident, proper removal of tumors of the parotid gland requires exposure of the facial nerve at its point of emergence from the stylomastoid foramen [*26*]. It can then be traced by careful dissection during the performance of subtotal parotidectomy. Recurrence after a properly performed operation for mixed tumor in competent hands should approximate zero. Nonetheless, patients who have had mixed tumors removed should be followed up at regular intervals because of the high recurrence rate (30 to 40 per cent) in average hands [*6,7*].

A correct diagnosis is essential to the proper intelligent management of any neoplasm. For many years we have insisted on a personal perusal of biopsy specimens of tissue removed elsewhere before treating a patient. Nowhere

in oncology is this principle more important than in the difficult area of neoplasms of the parotid gland. Even among experienced pathologists with many years of experience in this area, there are many differences of opinion. The wisdom of this personal evaluation of biopsy specimens is well illustrated in our case. Correct interpretation of the first lesion in the case reported herein enabled us to avoid the disfiguring radical surgery or prolonged radical radiation that would have been the proper management of an adenocarcinoma of the parotid gland.

SUMMARY

1. Bilateral mixed tumors of the parotid salivary gland are rare.

2. The tenth case of bilateral mixed tumor of the parotid salivary gland is reported and added to the medical literature.

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The Value of Liver Function Tests

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THERE is disagreement as to the diagnostic value of liver function tests, particularly in surgical patients. However, it is our impression that they can be of great value providing proper interpretation is placed on their results. Very important is the fact that the liver performs a multitude of functions, and no one test will yield data on them all. For this reason it is necessary to use more than one test if maximum information is to be derived.

Before proper interpretation can be placed on the results of these laboratory aids, we must keep in mind the significance of the respective tests. In general, the purpose of the thymol turbidity and cephalin flocculation tests is to detect quantitative and possibility qualitative changes in the serum albumin and globulin (primarily gamma fraction). These protein alterations result from hepatocellular inflammation or breakdown. Accordingly, the results of these tests should not be positive unless cellular damage is present. The enzyme alkaline phosphatase is excreted in the bile and likely is in part produced by the liver. Bile duct or biliary radicle obstruction and occasionally hepatocellular disease (possibly relating to increased production of the enzyme) thus may give rise to elevations. A number of authors have indicated the usefulness of the alkaline phosphatase determination in the detection of metastatic hepatic neoplastic disease. Hyperbilirubinemia results either from inability of the hepatic cell to pass enough of the bile pigment into the biliary radicles or from obstruction of the biliary outflow. Abnormal albumin/globulin ratios, as they apply to liver disease, are generally the result of long-standing hepatic dysfunction. The failing ability of the liver to produce albumin plus the appearance of increased amounts of serum globulin account for this finding. For this reason, as a rule, one expects albumin/globulin ratio determinations to be abnormal frequently in patients with cirrhosis. An increased prothrombin time may be due to one of two causes: the inability of the liver to synthezise prothrombin because of cellular abnormality or diminished vitamin K absorption secondary to lack of bile in the intestine. Because hepatic parenchymal or obstructive disease commonly causes the prothrombin time to be abnormal, this test is of relatively little value diagnostically but remains an important laboratory procedure in the management of patients with hepatobiliary disease.

The Bromsulphalein® test deserves special mention. This test is one of the simplest, most sensitive and reliable tests of hepatic function in the patient without jaundice. The Bromsulphalein test is a measure of both the blood flow through the liver and the excretory capacity of the liver cell. Accordingly, parenchymal inflammation and edema (hepatitis), inflammation and fibrosis (cirrhosis), and replacement of the liver tissue by tumor should result in abnormal retention. Unfortunately, the Bromsulphalein test is of little diagnostic value in the presence of jaundice, and attempts to correct the result taking into consideration the presence of icterus have not proved of value.

Care must be taken in the interpretation of the results of liver function tests to exclude causes other than hepatobiliary disease for abnormal values. For example, an elevation of the alkaline phosphatase may result from osseous disease and hyperbilirubinemia may be secondary to hemolytic states, both of these being independent of liver function.

CLINICAL MATERIAL

Our purpose in this presentation is to evaluate our experience with liver function tests in 224 patients with established hepatobiliary disease. We have elected to record our data under various diagnostic headings which were

TABLE I

RESULTS OF LIVER FUNCTION TESTS IN PATIENTS WITH ESTABLISHED DIAGNOSES OF HEPATOBILIARY DISEASE

	Cirrhosis	Cirrhosis with Varices	Portal Vein Thrombosis	Viral Hepatitis	Primary Hepatic Neoplasm	Metastatic Hepatic Neoplasm	Stone in Common Bile Duct	Carcinoma of Head of Pancreas	Carcinoma of Ampulla of Vater	Carcinoma of Common Bile Duct
Number of patients	54	21	6	48	16	16	31	40	4	9
Jaundice	41%	26%	0%	94%	31%	7%	71%	100%	100%	100%
Hyperbilirubinemia	84%	72%	0%	98%	62%	38%	76%	100%	100%	100%
Average (mg./100 ml. serum)	5.5	2.4	0.5	10.3	5.5	1.3	8.0	18.1	12.7	25.6
Moderate elevation	90%	100%	0%	81%	87%	100%	77%	41%	75%	11%
Marked elevation	10%	0%	0%	19%	13%	0%	23%	59%	25%	89%
Hypoalbuminemia	51%	40%	0%	77%	53%	29%	10%	16%	0%	11%
Hyperglobulinemia	45%	95%	0%	14%	13%	21%	0%	16%	25%	22%
Reversed albumin/globulin ratio	53%	40%	0%	7%	13%	14%	0%	13%	0%	22%
Abnormal thymol turbidity test	81%	90%	0%	98%	53%	20%	41%	28%	50%	44%
Average (units)	10.8	9.1	1.8	21.7	9.3	3.2	4.3	3.8	5.7	5.2
Moderate elevation	70%	89%	0%	35%	63%	100%	100%	91%	100%	100%
Marked elevation	30%	11%	0%	65%	37%	0%	0%	9%	0%	0%
Abnormal cephalin flocculation test	61%	57%	0%	88%	40%	13%	3%	8%	0%	0%
Moderate abnormality	39%	42%	0%	12%	50%	100%	0%	100%	0%	0%
Marked abnormality	61%	58%	0%	88%	50%	0%	100%	0%	0%	0%
Abnormal Bromsulphalein	95%	94%	0%	84%	100%	70%	100%	93%	100%	100%
Average (%)	28.1	27.7	3.0	22.3	27.3	20.6	31.8	33.7	50.2	62.8
Moderate elevation	28%	30%	0%	43%	38%	43%	8%	0%	0%	0%
Marked elevation	72%	70%	0%	57%	62%	57%	92%	100%	100%	100%
Elevated alkaline phosphatase	25%	30%	....	49%	40%	55%	79%	95%	75%	100%
Average (Bodansky units)	4.7	5.8	....	5.5	6.2	8.4	10.7	13.0	12.5	10.4
Moderate elevation	66%	50%	....	100%	83%	80%	70%	81%	66%	100%
Marked elevation	33%	50%	....	0%	17%	20%	30%	19%	33%	0%
Abnormal prothrombin time	82%	75%	66%	52%	50%	73%	59%	53%	33%	37%

established before the patient's discharge from the hospital: Cirrhosis (fifty-four patients); patients with cirrhosis demonstrated to have esophageal varices (twenty-one patients); viral hepatitis (forty-eight patients); calculus in common duct (thirty-one patients); carcinoma of the pancreatic head (forty patients); primary hepatic neoplasms (sixteen patients); malignant neoplasms metastatic to the liver (sixteen patients); carcinoma of the ampulla of Vater (four patients); carcinoma of the common duct (nine patients); and portal vein thrombosis (six patients).

Cases were selected for inclusion in the study on the basis of: the presence of an established diagnosis, the availability of the record for review and the fact that several tests had been performed. Instances of questionable diagnoses

TABLE II
RESULTS OF LIVER FUNCTION TESTS IN PATIENTS WITH HEPATIC PARENCHYMAL DISEASE AND EXTRAHEPATIC BILIARY OBSTRUCTION

	Cirrhosis (54 Patients)	Viral Hepatitis (48 Patients)	Extrahepatic Obstruction (84 Patients)
Hyperbilirubinemia..	84%	98%	91%
With jaundice....	41%	94%	90%
Albumin/globulin ratio reversal.....	53%	7%	9%
Thymol turbidity elevation.....	81%	98%	36%
Cephalin flocculation abnormality.....	61%	88%	5%
Alkaline phosphatase elevation.....	25%	49%	89%
Abnormal Bromsulphalein retention..	95%	84%	97%

as expressed by the managing physicians were rejected. The results of tests performed soon after admission are usually more important than those performed later because treatment should tend to correct hepatic dysfunction and thus reduce the degree of positive findings. Although the results of the initial tests after hospitalization are recorded here, the desirability and usefulness of performing serial determinations in many instances of clinical practice is not questioned.

"Normal" and "abnormal" results were stated to exist on the basis of the schedule to follow. In an attempt to define "abnormal" more accurately as to extent, the terms "moderate" or "marked" have been used to indicate the degree of abnormality.

Serum albumin: 3.4 to 5.2 gm./100 ml. serum.

Serum globulin: 2.0 to 3.5 gm./100 ml. serum.

Serum bilirubin: 1.0 mg./100 ml. serum, or below, is considered normal; moderate elevation, 1.1 to 15.0 mg./100 ml. serum; marked elevation, above 15 mg./100 ml. serum.

Cephalin flocculation test: 0. to 1 plus is considered normal; moderately abnormal, 2 plus to 3 plus; markedly abnormal, 3 plus to 4 plus.

Thymol turbidity test: 0 to 4 units is considered normal; moderate elevation, 4.1 to 15.0 units; marked elevation, above 15 units.

Serum alkaline phosphatase: 2 to 5 Bodansky units (child 5 to 15 Bodansky units) is considered normal; moderate elevation, 5.0 to 15.0 Bodansky units; marked elevation, above 15 Bodansky units.

Prothrombin time: 75 per cent of normal or greater is considered normal.

Bromsulphalein: 5 per cent or less retention in 45 minutes is considered normal; moderate retention, 5.1 to 20.0 per cent retention; marked retention, above 20 per cent retention.

Serum Amylase: 80 to 150 Somogyi units is considered normal.

The results of the liver function tests are recorded in Tables I and II. The data are further considered hereafter.

RESULTS

Cirrhosis. In the series we encountered fifty-four patients with cirrhosis, all either proved by gross examination of the liver (ten patients) or histologic study (forty-four patients). The average age was forty-seven years, and 63 per cent of the patients were males. Of the group 56 per cent had an alcoholic history and slightly less than half were recorded as having clinically splenomegaly or ascites. Of the group 39 per cent had esophageal varices as shown by esophagoscopy or x-ray examination; however, not all patients were examined by these two methods, so the figure is low. One-third of the patients either had bleeding varices on admission or gave a history of having bled in the past. A long history was usual, averaging thirty months. Jaundice was present on admission in 41 per cent of the cases.

The liver function tests were consistently abnormal, only one patient having completely normal studies, and in that patient a Bromsulphalein test (the most accurate one for cirrhosis) had not been performed. The Bromsulphalein test was found to be the most reliable for detecting abnormal function, 95 per cent exhibiting abnormal retention and 72 per cent of these being to a marked degree. Elevation of the serum bilirubin was noted in 84 per cent, but in all except a few, to a minimal degree. A reversed albumin/globulin ratio was present in about half the patients, with 51 per cent having hypoalbuminemia and 45 per cent having an elevated globulin. The thymol turbidity test was more commonly abnormal than the cephalin flocculation, the incidence being 81 and 61 per cent, respectively. Fourteen per cent had normal cephalin and thymol tests, but all these had abnormal Bromsulphalein retention, again indicating the sensitivity of the latter test. The average alkaline phosphatase was normal, but 25 per cent had some degree of elevation, mostly minimal; an infrequent patient did, however, have rather marked elevation, one value of 26.1 Bodansky units having

been recorded. Over four-fifths of the patients had prothrombin times of less than 75 per cent of normal.

Cirrhosis with Proved Esophageal Varices. It was thought desirable to consider the patients with esophageal varices separately, because these represent a special group of cirrhotic patients most likely to be confronting the surgeon. Liver function tests may be of tremendous diagnostic aid when one is attempting to localize the cause of upper gastrointestinal bleeding, because patients with cirrhosis of a degree sufficient to produce bleeding varices will almost always have a positive Bromsulphalein test and often have an altered albumin/globulin ratio.

Twenty-one of the fifty-four patients with cirrhosis previously considered had varices. The average age was identical to that in the group of patients with cirrhosis as a whole, and the average duration of illness nearly so. Females predominated slightly. An alcoholic history was present in 43 per cent. Clinical ascites or splenomegaly was noted in 62 and 57 per cent, respectively. Of the group, 71 per cent of the patients either had bled or were bleeding on admission. Clinical jaundice was present in only one-fourth of the patients.

Liver function tests were abnormal in all twenty-one patients. They tended to follow the same general pattern as in the cirrhotic patients as a whole except that the incidence of hyperglobulinemia was higher (95 per cent as compared with 45 per cent). Similar findings were noted as regards the Bromsulphalein test (94 per cent abnormal), the high incidence of "chemical jaundice" (72 per cent of bilirubins elevated), and the greater frequency of thymol abnormalities as compared to cephalin flocculation.

Thus, in this group of patients, the cirrhotic patients as a whole and those with varices differed little when the data were compared, the only significant difference being the considerably greater incidence of hyperglobulinemia in those with the proved varix.

Portal Vein Thrombosis. We decided to include these patients in our study because the patient often presents with the sequelae of esophageal varices, and the question of the etiology of the portal hypertension arises. More commonly varices are secondary to cirrhosis; in this group liver function tests are invariably abnormal. We would expect liver function tests to be normal in most patients with portal vein thrombosis, and if true, these tests would be of considerable diagnostic value in patients with varices.

Six patients with portal vein thrombosis, all proved at celiotomy, are available for study. The average age was twenty-three years, and females dominated four to two. The patients had long histories, averaging five years. All had bled or were bleeding from the varices. None had jaundice.

Liver function tests, excluding prothrombin times, were normal. Alkaline phosphatase levels were determined in only two of the patients, and one had a borderline elevation. The prothrombin times were less than 75 per cent of normal in four of the six patients. In contrast to the patients with cirrhosis, none of these patients had Bromsulphalein retention. These tests clearly separate these patients from those in the cirrhotic group.

Hepatitis. Of the entire group, we encountered forty-eight patients with "viral" hepatitis. No case was proved histologically because none of the patients were operated on. However, all were hospitalized, many for prolonged periods, and at the conclusion of their period of confinement diagnosis was made without reservation as such. Any instance of questionable diagnosis was not included.

As would be expected, the average age was low, thirty years, but the range was wide, four to sixty-five years. Males and females were afflicted with essentially equal frequency. The average duration of illness was three weeks prior to hospitalization; 94 per cent had jaundice.

Liver function tests were abnormal in all patients. As the incidence of jaundice would suggest, almost all had elevated bilirubins (98 per cent) with the average being 10.3 mg./100 ml. serum and 81 per cent being less than 15.0 mg./ml. serum. Abnormal serum protein values were uncommon with albumin/globulin reversal in only 7 per cent. This supports the supposition that abnormal albumin/globulin ratios are seldom encountered except in chronic hepatic dysfunction. Abnormalities in thymol turbidity were present in 98 per cent, with 65 per cent having a thymol turbidity of greater than 15.0 units. Somewhat less commonly abnormal were the results of the cephalin flocculation tests (88 per cent positive), but when positive they tended to be markedly so. Almost one-half the patients with hepatitis had

mild elevations of alkaline phosphatase, the highest being 15.0 Bodansky units and the average 5.5. Only four of the forty-eight had phosphatase determinations in excess of 10 Bodansky units. As will be discussed later, because of the high incidence of jaundice, a high incidence of Bromsulphalein retention would be expected and was found in 84 per cent. The only patient in whom both the thymol and cephalin flocculation tests were normal was found to have marked Bromsulphalein retention.

Calculus in Common Duct. All proved surgically, thirty-one patients with choledocholithiasis were reviewed. The average age was fifty-five years, and women constituted 71 per cent of the group. On the average, symptoms had been present about one year; 71 per cent had jaundice on admission.

Three-quarters had an elevated serum bilirubin, the average being 8.0 mg./100 ml. serum and 77 per cent being less than 15.0 mg./100 ml. serum. Abnormal serum proteins, except for a 10 per cent incidence of hypoalbuminemia, were not found. No patient had a reversed albumin/globulin ratio. A moderate number had an elevated thymol turbidity test (41 per cent), but none were markedly so and the average was only 4.3 units. Only one patient had more than a 1 plus positive cephalin flocculation at forty-eight hours. Seventy-nine per cent of the patients had an elevated alkaline phosphatase, the average being 10.7 Bodansky units. The phosphatase determinations did not tend to be very high; only 30 per cent of the abnormal ones were over 15.0 Bodansky units, and only one patient had a value over 25.0 Bodansky units. Abnormal Bromsulphalein retention was noted in 100 per cent of the patients; however, since jaundice itself is associated with a high Bromsulphalein reading, this finding must be discounted considerably. Of the group, 59 per cent had an abnormal prothrombin time and 15 per cent had a mildly elevated blood amylase.

Carcinoma of the Pancreatic Head. Of our patients with carcinoma of the head of the pancreas, forty had enough liver function tests to justify inclusion in this study. All patients were diagnosed at celiotomy and biopsy was performed in 48 per cent. The average patient was sixty years of age; 58 per cent were males. The average duration of the symptoms prior to hospitalization was three months; all patients had jaundice on admission.

In keeping with the universal jaundice, 100 per cent had an elevated bilirubin, over half being to a marked degree. Elevated serum globulins and depressed serum albumins were both noted in the incidence of 16 per cent; 13 per cent had a reversed albumin/globulin ratio. The average thymol turbidity test was normal, but 28 per cent had elevations, the majority of which were minimal. Only 8 per cent had abnormal cephalin flocculation tests and none was more positive than "2 plus at forty-eight hours." The alkaline phosphatase readings were high in 95 per cent of the patients, the average being 13.0 Bodansky units. Only four patients had phosphatase levels in excess of 25.0 Bodansky units; the highest value was 68.7 Bodansky units. Bromsulphalein retention was found in 93 per cent of the patients, and all these had marked retention. The latter relates to the incidence of icterus. Slightly over one-half had an abnormal prothrombin time. Amylase determinations were performed in about half of the patients, and in this group 38 per cent had elevations, all minimal.

An attempt was made to ascertain the incidence of duodenal abnormalities on x-ray examination. Only about half were so studied, but the incidence of some abnormality being found in those examined was 38 per cent. Most had either a distorted or displaced duodenal loop.

Carcinoma of the Ampulla of Vater. Of the patients with carcinoma of the ampulla, only four had sufficient data in their charts to warrant conclusions. Three underwent resection and one a biopsy. The age range was fifty-six to sixty-nine years, with an average of sixty-two. Men and women were equal in number. All had jaundice on admission; the average duration of symptoms was four and a half months.

Because of the small number, average figures are of little value, but the following was noted: Moderate bilirubinemia was universal, the average determination being 12.7 mg./100 ml. serum. The only serum protein abnormality was the presence of a high globulin in one patient. One-half had mildly elevated thymol tests. None of the four had positive cephalin tests. Three of the four had elevated alkaline phosphatase ranging from 6.5 to 28.3 Bodansky units. Only one patient was tested for Bromsulphalein retention, and marked retention was revealed. One patient of three tested had an abnormal prothrombin time. Upper gastrointestinal x-ray films were normal in each instance.

Carcinoma of the Common Bile Duct. There were seven patients with carcinoma of the common bile duct. In addition we have included one patient with carcinoma of the gallbladder and one with carcinoma of the porta hepatis (primary unknown) because in both of these there was complete obstruction of the common duct. All lesions were visualized at surgery, all but one proved histologically, and two of the common duct lesions were resected. The average age was sixty-seven years, and men predominated five to four. All had jaundice and gave a history averaging four months in duration.

The serum bilirubin was elevated in every patient, and in 89 per cent to a marked degree. The average bilirubin was 25.6 mg./100 ml. serum and seven of the nine were in excess of 20.0 mg./100 ml. serum. Hypoalbuminemia was noted in one patient and hyperglobulinemia in two. Four of the nine had mild thymol elevations but none had an abnormal cephalin flocculation test. All had an elevated serum alkaline phosphatase test, but none was markedly so, the highest being 14.9 Bodansky units. The Bromsulphalein test revealed marked retention, averaging 62.8 per cent in the four patients tested. Over one-third had abnormal prothrombin times.

Primary Hepatic Neoplasm. Included are sixteen patients with histologically proved primary hepatic malignant neoplasm. There were two sarcomas and the remainder were carcinomas. Four of the patients with carcinoma also had cirrhosis. Nine months was the average duration of symptoms prior to hospitalization. Five of the sixteen patients had jaundice.

Hyperbilirubinemia was encountered in 62 per cent, only one patient having a marked elevation. Hypoalbuminemia was encountered in over half the patients and one had an elevated globulin. Thymol turbidity elevations were present in eight of fifteen patients tested. Six had cephalin flocculation abnormalities, this test being strongly positive in three instances. The patients with the coexisting cirrhosis tended to have the abnormal cephalin and thymol tests; 40 per cent had alkaline phosphatase elevations, almost all moderately so. A Bromsulphalein test was performed in only eight of the patients but was abnormal in every case. The retention tended to be marked, averaging 27.3 per cent. One-half had abnormal prothrombin times.

Metastatic Carcinoma of the Liver. Although metastases to the liver are common, it is not routine to perform complete "liver profiles" on all such patients; only sixteen patients had sufficient data to justify inclusion in this study. The primary lesions were mostly gastrointestinal and the secondary lesions, all proved at celiotomy, varied from small to large in size. The average age was fifty-four, the males predominating nine to seven. On the average, the onset of illness dated seven and a half months prior to admission. Only one patient had jaundice.

In spite of the low incidence of jaundice, 38 per cent had an elevated serum bilirubin, exclusively to a mild degree. Of the group, 29 per cent had hypoalbuminemia and 21 per cent had an elevated serum globulin. Abnormal thymol and cephalin flocculation tests were noted in 20 and 13 per cent, respectively, all abnormalities being to a mild degree. Nine patients had a serum alkaline phosphatase determination; five results were abnormal, only one markedly so. Ten Bromsulphalein determinations were performed and seven exhibited retention. The average Bromsulphalein retention was 20.6 per cent. Almost three-fourths of the patients had abnormal prothrombin times.

Value of the Bromsulphalein Test in Jaundice. It was decided on the basis of the foregoing data to evaluate the relationship of jaundice to the Bromsulphalein test. How often is the Bromsulphalein test normal in a patient with jaundice? The patients who had jaundice secondary to any of the pathologic states considered were listed (seventy-six in number) and their Bromsulphalein values noted. Only four Bromsulphalein tests in the seventy-six patients were normal. The Bromsulphalein test appears to be of very little diagnostic value in the presence of jaundice.

SUMMARY

In this survey we have studied the results of several liver function tests, particularly the thymol, cephalin, prothrombin, Bromsulphalein, albumin/globulin ratio and alkaline phosphatase tests. Most of the diseases studied were surgical, but some important non-surgical diseases such as viral hepatitis and cirrhosis have been included. In patients with cirrhosis the three important features were: (1) Bromsulphalein retention in 95 per cent, with the majority being marked; (2) a reversed albumin/globulin ratio in 53 per cent; and (3) an elevated

thymol turbidity in 81 per cent. Cirrhotic patients with varices were found to have a higher incidence of hyperglobulinemia than those in the cirrhotic group as a whole.

Patients with portal vein thrombosis were included because they often present indirectly with bleeding esophageal varices, and the differential diagnosis arises with the more common etiologic factor, cirrhosis. The liver function tests in this study clearly separated these patients from those with cirrhosis, since test results were normal, with the exception that two-thirds of the patients with venous thromboses had an abnormal prothrombin time.

Like the other major category of hepatic parenchymal disease (cirrhosis), all patients with viral hepatitis had abnormal tests. The most significant feature was the fact that the thymol test was elevated in 98 per cent of the patients and markedly so in two-thirds; in 88 per cent of the patients in this group the cephalin flocculation test was positive. Only 7 per cent had an abnormal albumin/globulin ratio. Minimal elevations of the alkaline phosphatase were common.

The primary neoplasms of the liver, most of which were carcinomas, were associated in four instances with coexisting cirrhosis. The only constant observation was that all patients tested had significant Bromsulphalein retention, most to a marked degree. Hypoalbuminemia was common. In about half, the prothrombin test and either the thymol or cephalin tests were positive.

In metastatic hepatic neoplastic disease the most prominent finding was Bromsulphalein retention in seven of ten patients tested. In five of nine patients the alkaline phosphatase test was abnormal, but usually to a minimal degree.

The eighty-four patients with extrahepatic obstruction of the biliary tract from all causes can be considered together because they had similar tests results, the type of obstruction causing variation only in degree. The single most noteworthy finding was an 89 per cent incidence of alkaline phosphatase elevation, associated with only a 5 per cent occurrence of cephalin flocculation abnormality. Popper has mentioned this finding and it appears to be a significant one. Table II considers all patients with obstructive disease as a single group and permits comparison with the two major patient groups having primary parenchymal disease.

Several additional facts are apparent from this study: (1) In no group of patients was the cephalin flocculation abnormal as often as the thymol turbidity. This fact is indicative of the comparatively greater sensitivity of the latter over the former. In our patients with primary parenchymal disease both these tests were positive in a high incidence, but in patients with obstructive disease the cephalin flocculation was uncommonly positive and the thymol only occasionally so. (2) The Bromsulphalein test was noted to be of little diagnostic value in the presence of jaundice, almost all such patients having predictable retention. (3) A significant incidence of prothrombin time abnormality was noted in every type of disease process considered and was, therefore, of very little diagnostic value.

From these data we conclude that liver function tests have been of definite diagnostic value to us, particularly in differentiating intrahepatic disease from extrahepatic obstruction. The thymol was a reliable test of hepatic parenchymal disease. The cephalin flocculation was found to be of great value in excluding primary parenchymal disease in patients with obstruction of the extrahepatic biliary system. Serum alkaline phosphatase values were evaluated in at least three-quarters of patients with extrahepatic obstruction. The Bromsulphalein test was the most frequently positive test in cirrhosis and was commonly so in hepatic neoplastic disease.

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Observations on the Surgical Treatment of Peptic Ulcer

A SIX-YEAR REVIEW OF 101 MALE PATIENTS

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THE rationale of the time-honored Hofmeister Polya resection of the stomach for peptic ulcer has been under sharp criticism for several years. Not all centers in which gastrectomy is performed will agree that this procedure is good measured in terms of persistent pain, ability to work, maintenance of weight, the dumping syndrome, vomiting and melena. The surgical answer to peptic ulcer has not yet been found.

The purpose of this study is to report the observations on 101 consecutive gastrectomies for peptic ulcer disease over a six-year period from January 1, 1951 to December 31, 1956, performed at a small Veterans Administration Hospital.

METHOD OF STUDY

Those gastrectomies for which a preoperative diagnosis of peptic ulcer was made, are used as the basis for this report. The clinical records on all patients were reviewed and information tabulated regarding: (1) number of different surgeons performing operations, (2) number of operations by years, (3) sex, (4) race, (5) average age at operation, (6) average duration of symptoms, (7) location of ulcer, (8) average preoperative hydrochloric acid values, (9) previous gastrointestinal surgery, (10) indications for surgery, (11) type of operation performed, (12) surgical complications and (13) deaths.

The following questionnaire was sent to each patient having undergone gastectomy for peptic ulcer and the answers tabulated:

1. Are you satisfied with your operation?
2. Are you having any pain?
3. Are you able to take a full diet, or must you keep on a limited one?
4. Have you gained or lost weight since you were here? How much?
5. Have you done any vomiting since operation? Have you vomited blood or passed blood?
6. Are you working? If you are not working, is it because of stomach trouble?
7. Has it been necessary for your family physician to see you at all since you were operated upon?
8. Are you absolutely free of trouble since your operation?

All patients operated upon were men. (Table 1.) The youngest patient was twenty-four and the oldest was sixty-six years of age. Ninety-nine were white and two were Negro. The average period of duration of symptoms

TABLE 1

No. of surgeons performing operations	8
No. of operations by year (total—101):	
1951	20
1952	23
1953	16
1954	14
1955	14
1956	14
No. of patients by race:	
White	99
Negro	2
Average age at operation	40 years
Youngest	24 years
Oldest	66 years
Average duration of symptoms	8 years

TABLE II
NORMAL VALUES OF HYDROCHLORIC ACID

Data	Response per Ten-Minute Sample			
	Fasting	Alcohol or Broth Meal	Injection of Histamine	Insulin Hypoglycemia
Volume of gastric secretion (ml.)	10–50*	10–25	10–25	15–30
Free acid (units)	0–30	20–40	70–125	50–110
Total acids (units)	5–40	30–50	80–130	60–115

*Total content.

was eight years. The average age at time of surgery was forty years.

Pathological reports recorded the ulcer as being duodenal in eighty-eight cases, and gastric in thirteen. There were no cases of gastroduodenal ulcer.

Gastric analysis for free and total acidity was made in forty-seven of the cases preoperatively. The average value for free hydrochloric acid was 39.2 clinical units and for total hydrochloric acid 57 clinical units. The normal values for hydrochloric acid used in our hospital are listed in Table II.

The period of survey was six years from January 1, 1951 to December 31, 1956. One hundred one cases were reviewed. Of the 101 questionnaires sent out, sixty-two responses were obtained, thirty-nine were lost to follow-up. There was one death in the entire series.

PREVIOUS GASTROINTESTINAL SURGERY

Acute perforations of peptic ulcer were closed in twenty-one patients as a separate procedure prior to the decision to perform gastrectomy. In one patient gastrectomy was attempted but blood loss from gastrointestinal hemorrhage made further surgery not feasible. Gastrectomy was performed later. In another patient enterostomy for feeding purposes was carried out on February 26, 1953. Another operation for release of intestinal obstruction was performed on March 5, 1953 and finally subtotal gastrectomy was performed on April 2, 1953. In yet another patient, a twenty-six year old man, the stomach and duodenum were explored in 1955 for the source of massive bleeding. No cause could be found. One year later gastrectomy was carried out for massive bleeding from a duodenal ulcer.

TABLE III
INDICATIONS FOR SURGERY AND RESULTS
(SIXTY-TWO CASES)

Condition	No. of Cases and Per cent of Total	Followed-up (No. of Cases)	Excellent (%)	Good (%)	Poor (%)
Obstruction	19 (30.6)	9	56	22	22
Perforation	16 (25.8)	9	56	22	22
Repeated hemorrhage	40 (64.5)	25	20	36	40
Intractable pain	39 (62.9)	19	37	32	32
Massive hemorrhage	42	25	40	28	32
Controllable	29 (48.3)	23	39	26	39
Uncontrollable	13 (18.3)	2	50	50	0
			42	28	30

INDICATIONS FOR SURGERY

Massive hemorrhages, controllable and uncontrollable, forty-two in number, led the list of indications for surgery. (Table III.) Repeated hemorrhage was present in forty cases, intractible pain in thirty-nine, obstruction in nineteen and history of perforations in sixteen. More than one indication was present in an appreciable number of cases.

TYPE OF OPERATION

Ninety-one patients had 75 per cent of the stomach removed. The remainder had slightly more or less. The ulcer was removed in every case. The antrum was removed in every case. In nineteen cases an antecolic anastomosis was made whereas in seventy-two cases retrocolic anastomosis was executed. The Hofmeister isoperistaltic anastomosis was carried out in ninety-two cases. In nine cases the Billroth I procedure was followed. Vagotomy was performed at time of surgery in ten patients.

MORBIDITY AND MORTALITY

One patient had a wound abscess. Two patients had wound dehiscences and one patient had intestinal obstruction following surgery. In four cases postoperative hemorrhage occurred within twenty-four hours of surgery. Three of these patients were explored and one was treated conservatively. There were no hospital deaths and one patient died a year later of electrocution while operating an electric lawn mower. (Table IV.)

RESULTS

Sixty-two patients answered the questionnaire sent them (Tables III and V.) Of this

TABLE IV
SUMMARY OF RESULTS

Results	No. of Cases
Died in hospital	0
Died later	1
Recurrent bleeding (17):	
Rectal	16
Hematemesis	1

TABLE V
SUMMARY OF RESULTS (SUBJECTIVE)

Results	Per cent
Total number of responses (62)	....
Patients satisfied	87
Relieved of pain	54.8
Clinically free of symptoms	59.6
Under medical care (postoperatively)	66.0
Able to work	74.2
Maintains or gains weight	67.7
Dumping syndrome	12.9
Vomiting	37.0

number 87 per cent stated they were satisfied with their operation, 54.8 per cent were relieved of pain and 59.6 per cent were clinically free of symptoms at the time of this survey. Sixty-six per cent stated that they were under medical care but considerably less than this percentage were under supervision for symptoms relating to their surgery. Of the sixty-two patients, 74.2 per cent were able to work, 67.7 per cent had either maintained or increased their preoperative weight [4], 12.9 per cent complained of mild symptoms of the "dumping syndrome" and 37 per cent had vomiting of mild to moderate degree.

The results were based on various combinations of answers to the questionnaire and classified as excellent, good and poor.

For all indications, 42 per cent received a score of excellent, 28 per cent good and 30 per cent poor. By itemizing indications it was noted that of those patients with obstructions, nine were followed up with 65 per cent excellent, 13 per cent good and 22 per cent poor results. Of those with a history of perforation, nine were followed up with 56 per cent excellent, 22 per cent good and 22 per cent poor results.

For the twenty-five patients with repeated hemorrhage who were followed up, the results were excellent in 20 per cent of the cases, good in 40 per cent and poor in 40 per cent. Of the nineteen patients with intractable pain who were followed up, 37 per cent had excellent results, 32 per cent good results and 32 per cent poor results. For the twenty-five patients with massive hemorrhaging who were followed up, 40 per cent of the results were excellent, 28 per cent good and 32 per cent poor. For the twenty-three patients with controllable hemorrhage who were followed up, the results were excellent in 35 per cent of the cases, good in 26 per cent and poor in 39 per cent. Of the two patients with uncontrollable hemorrhage who were followed up, one had an excellent and one a good result. No patients with hemorrhage died of peptic ulcer disease.

COMMENTS

Careful screening of indications for surgery together with the type of operative procedure used appear to be important factors in the over-all results following gastrectomy for peptic ulcer disease [3].

Since only sixty-two of the questionnaires sent out were answered, it is believed that the group of patients covered were itinerant and difficult to contact. Even though eight different surgeons performed the gastrectomies there is a striking uniformity in the technique and care, thus facilitating uniform results. The figure of 16.8 gastrectomies per year for six consecutive years attests to the conservative well thought out evaluation of each case. The subjects' average age of forty years is in conformity with most series reported elsewhere. Of the sixty-two patients who responded to inquiry, forty-six were still able to work following gastrectomy and only sixteen were disabled and unable to work because of surgery. This 74 per cent employed, however, is not a true figure because of the 38 per cent who could not be contacted. Marital status and race are unimportant in this review.

The average duration of preoperative symptoms was eight years. This only means that some patients had numerous hospitalizations for peptic ulcer, were responsive to medical therapy and only came to surgery when the symptoms of perforation, obstruction, massive hemorrhage or intractable pain developed [1]. A further implication is that a sizable number either did not stay on their diet and/or were

addicted to alcohol and smoked. This is always a difficult problem in this series of patients. It is interesting to note that 88 per cent of the ulcers were duodenal, none were gastroduodenal, and *all* the remaining 13 per cent (gastric) were benign on microscopic section.

Leading in the indications for surgery was massive hemorrhage (41 per cent), followed closely by repeated hemorrhages (40 per cent) and intractable pain (39 per cent). The cases of controllable hemorrhage totaled 29 per cent and uncontrollable hemorrhage 12 per cent. Uncontrollable is interpreted as hemorrhage which cannot be controlled except by emergency surgery and ligation of the bleeder, transduodenally, or by subtotal gastrectomy. The remaining controllable group can be treated by transfusion and the ulcer located preoperatively by gastrointestinal x-ray series. Perforations (16 per cent) varied from one to two. The tendency has been to operate after the second perforation. A complication at the time of surgery was massive uncontrollable hemorrhage (13 per cent) which constituted the greatest surgical risk. These patients should have been operated upon following previous massive hemorrhage.

The recurrent bleeding (17 per cent of the indications, 16 per cent being melena and 1 per cent hematemesis) must be attributed to residual gastritis of the "left in" pouch of stomach [4]. Here again cooperation of the patient regarding diet and later care is a rather dubious matter.

As to subjective results, 87 per cent of the patients said they were satisfied with the operation but only 54 per cent were relieved of pain. The pain must be attributed to lack of cooperation on diet—59 per cent of the patients were declared clinically free of symptoms based principally on whether or not they were able to work, if they were under medical care or relieved of pain. Strangely enough 66 per cent were under medical care following surgery. This must be a *bona fide* result in most cases. Sixty-eight per cent were able to maintain or regain their preoperative weight. This is not a good result and therefore it is questioned whether removal of the antrum and 75 per cent of the stomach is indicated. Vomiting as a follow-up symptom was noticed in 37 per cent of the patients. This also represents not all of what should be expected from gastrectomy.

CONCLUSIONS

Consideration should be given to gastrectomy following the first massive hemorrhage in a patient fifty years old or older.

Surgery should be seriously considered following the first perforation in a man fifty years of age or older.

"Blind" gastrectomy should be performed for massive gastrointestinal hemorrhage if the cause cannot otherwise be found.

A departure from the time-honored Hofmeister procedure should be considered, such as the "antral exclusion" operation of Waddell and Bartlett to include vagotomy [2]. The removal of more than 50 per cent of the stomach is open to question.

SUMMARY

1. One hundred one consecutive gastrectomies for peptic ulcer are reviewed, covering a period of six years.

2. Sixty-two responses to inquiry were received.

3. Data includes: (1) surgeon, year, sex, age at operation, occupation, marital status, race, duration of ulcer; (2) indications for surgery; (3) complications of surgery; (4) history of previous gastrointestinal surgery; (5) type of resection; (6) preoperative gastric acidity; (7) later surgery, and (8) results (objective and subjective).

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Postoperative Complications in the Elderly Surgical Patient

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ALTHOUGH a great deal has been written about the elderly surgical patient, the literature deals primarily with mortality and preoperative and postoperative care. Comparatively little information is available concerning postoperative complications in this group of patients. The need for such a study became apparent after it was recently shown on this surgical service that the incidence of postoperative complications increases considerably in patients sixty years of age and over [4]. It was also shown that one of three major operations during 1955 was performed upon a patient sixty years of age or over, adding further importance to such an investigation. This report is concerned primarily with complications following major operations in patients of advanced years.

METHODS

The charts of patients sixty years of age or older having surgery performed on the general surgical service during 1955 were reviewed. One standard comprehensive list of complications was applied to all of the charts studied. Each record was examined completely and many additional complications were discovered which had not been recorded originally, either by oversight or by lack of a uniform definition of a postoperative complication. Any complication occurring during a patient's hospital stay was included regardless of the length of time after operation. The specialties of orthopedics, neurosurgery, urology, gynecology and plastic and thoracic surgery were not included.

During 1955 there were 723 operations performed upon patients sixty years of age or older on the general surgical service. Of 532 major operations, 184 (35 per cent) were followed by one or more complications. In comparison, of 1,169 major operations upon patients under sixty years of age during the same period, 272 (23 per cent) were followed by one or more complications. Of the minor operations performed upon elderly patients, 11 per cent resulted in one or more complications, while only 4 per cent of minor operations upon younger patients were followed by complications.

There were forty-five deaths following the 532 major operations in the elderly age group, giving a postoperative mortality of 8.5 per cent. In patients under sixty years of age who had major operations during this time the postoperative mortality was 4 per cent. Pulmonary complications were present in about half of the elderly patients who died. Wound, urinary and miscellaneous complications occurred in only a few patients who died.

No effort was made to divide these operations into emergency or elective procedures. It is, of course, well known that the mortality and morbidity rates following emergency surgery in elderly patients are much higher than those following elective surgery [1,2].

INFLUENCE OF SEX AND ECONOMIC STATUS ON POSTOPERATIVE COMPLICATIONS

Of the 532 major operations, 296 were performed upon males and 236 upon females. Thirty-nine per cent of the males operated upon had postoperative complications compared to only 29 per cent of the females.

Major operations performed by the resident

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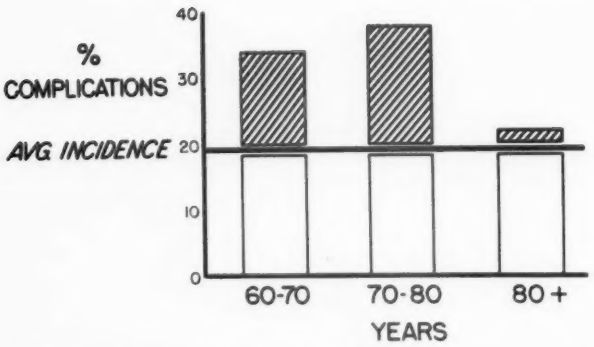

FIG. 1. Postoperative complications. Incidence in patients over sixty years of age.

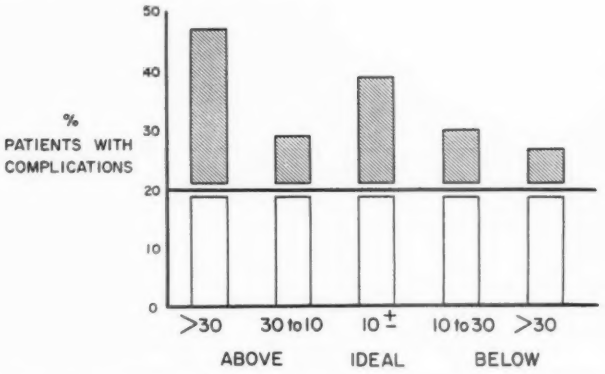

FIG. 2. Influence of weight on postoperative complications.

staff numbered 220, and the private attending staff accounted for 312. Thirty-seven per cent of the elderly patients operated upon by the resident staff had postoperative complications, while 33 per cent operated upon by the private staff had complications.

COMPLICATIONS BY AGE

Of the 309 major operations performed upon patients between sixty and sixty-nine years of age 105 (34 per cent) resulted in at least one postoperative complication. (Fig. 1.) One hundred eighty-two major operations were performed upon patients between seventy and seventy-nine years of age, of which seventy (38 per cent) were followed by complications. There were forty-one major operations upon patients who were eighty years of age or over. Nine of these operations resulted in complications for an incidence of 22 per cent.

INFLUENCE OF WEIGHT ON POSTOPERATIVE COMPLICATIONS

It was possible to calculate the ideal weight of 456 patients sixty years of age or over who underwent major operations. Of 170 patients whose actual weight was within 10 per cent of the calculated ideal weight, 39 per cent had one or more complications. (Fig. 2.) In 115 patients whose actual weight was between 10 and 30 per cent above ideal weight, 29 per cent had postoperative complications. There were fifty-one patients who were 30 per cent or more above ideal weight, of which 47 per cent had complications. The 105 operations upon patients whose actual weight was between 10 and 30 per cent below the calculated ideal weight had a complication rate of 30 per cent. While there were only fifteen patients whose actual weight was more than 30 per cent below ideal weight, complications followed operation in 27 per cent. This latter group is exceedingly small and the results are not statistically significant.

These figures agree fairly well with recent studies [4] on this surgical service which have shown that there is no significant increase in the incidence of postoperative complications until the patient's actual weight is 30 per cent above or below the ideal weight.

CLASSIFICATION OF COMPLICATIONS

In all, 255 complications occurred after 184 major operations upon elderly patients. These complications were divided into six primary types: wound, gastrointestinal, pulmonary, cardiovascular, urinary and miscellaneous. (Fig. 3.)

One of four complications involved the wound. Wound abscess, excluding stitch abscess, was by far the most common complication in this group. Next were wound separations and wound hematomas, each of which was about half as frequent. The remainder of the wound complications encompassed a great variety of conditions. (Table I.) The incidence of wound complications was almost identical with that of patients under sixty years of age operated upon during the same period of time.

One of five complications that occurred in the elderly patient was of the gastrointestinal type. The intra-abdominal abscess was the most common of this group. (Table II.) Once again it is seen that infection plays a major role in today's postoperative problems.

One of six complications was classed in the pulmonary group and the most common was that of atelectasis. (Table III.) It was interesting to find that atelectasis occurred three times

TABLE I
WOUND COMPLICATIONS

Type of Complication	No. of Cases
Wound abscess	26
Wound separation	11
Wound hematoma	11
Skin graft failure	4
Necrosis of wound edges	3
Evisceration	2
Stitch abscess	2
Other wound complications	4
Total	63

TABLE II
GASTROINTESTINAL COMPLICATIONS

Type of Complication	No. of Cases
Intra-abdominal abscess	11
Obstruction at site of anastomosis	6
Gastrointestinal hemorrhage	6
Intraperitoneal hemorrhage	5
Enterocutaneous fistula	5
Persistent ileus	4
Generalized peritonitis	3
Mechanical obstruction	2
Pancreatitis	2
Other gastrointestinal complications	7
Total	51

TABLE III
PULMONARY COMPLICATIONS

Type of Complication	No. of Cases
Atelectasis	22
Pneumonitis	10
Pleural effusion	3
Pulmonary edema	2
Pneumothorax	2
Subcutaneous emphysema	1
Total	40

more frequently in the elderly patient than in patients under sixty years who were operated upon during this period. It was also found that atelectasis was four times more frequent in the elderly male than it was in the elderly female patient. The overweight patients had slightly more atelectasis than the patients of normal weight, but four times more than the underweight patients.

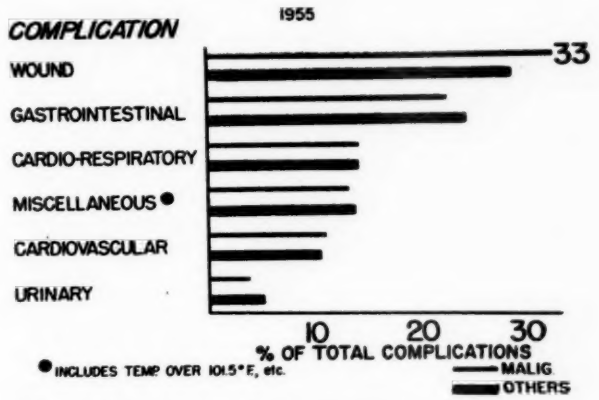

FIG. 3. Postoperative complications for the year 1955.

TABLE IV
CARDIOVASCULAR COMPLICATIONS

Type of Complication	No. of Cases
Thrombophlebitis	11
Pulmonary embolus, non-fatal	6
Pulmonary embolus, fatal	2
Peripheral embolus	5
Congestive heart failure	3
Unexplained shock	2
Cardiac arrhythmia	2
Heart block	1
Cerebrovascular accident	1
Coronary thrombosis	1
Mesenteric thrombosis	1
Other	3
Total	38

Cardiovascular complications comprised about 15 per cent of the total complications. Thrombophlebitis was the most common in this group. (Table IV.) Of the pulmonary emboli which occurred, one-fourth were fatal. During the year, for all ages, there were four cases of coronary thrombosis postoperatively, only one of which occurred in a patient who was sixty years of age or over.

Urinary complications accounted for only one of sixteen postoperative complications. The most common again was that of infection. (Table V.)

The miscellaneous complications were those conditions which could not be satisfactorily classified in the first five groups. They comprise 18 per cent of the total complications and the most common in this group was

TABLE V
URINARY COMPLICATIONS

Type of Complication	No. of Cases
Urinary infection	7
Uremia	4
Lower nephron nephrosis	4
Hydronephrosis	1
Total	16

TABLE VI
MISCELLANEOUS COMPLICATIONS

Type of Complication	No. of Cases
Unexplained temperature over 101.5°F.	34
Drug allergy	2
Psychosis	2
Septicemia	2
Operative rupture of spleen	1
Other	6
Total	47

unexplained temperature of over 101.5°F. orally. (Table VI.) The others in this group include a variety of conditions, some of which occurred without any significant frequency.

COMMENTS

This rather detailed examination of postoperative complications which occurred after 532 major operations upon patients sixty years of age or older has shown several interesting things. It was found that whereas the frequency of complications in this group of patients is significantly increased over those patients under sixty years of age, the elderly patient was not more prone to any particular type of complication. In other words, the percentage of wound, gastrointestinal, pulmonary, cardiovascular and urinary complications was approximately the same in patients under sixty years as it was in patients over sixty years of age.

Complications in the elderly male patient were more frequent than in the elderly female patient. Also, complications were more frequent in service patients than in private patients. The higher percentage of poor-risk patients on the clinical service probably explains in part this difference in complication rates.

Patients aged eighty years or above had a lower complication rate than those patients between sixty and eighty. It is believed that this could be due to the extent of surgery being tempered in these patients, or more thorough and critical care in the postoperative period because of the age or, as has been alluded to in the past, a patient this old may be constitutionally more sound.

Moderate obesity was not associated with a higher complication rate, but those patients whose weight was more than 30 per cent above the ideal level showed a marked increase in the rate of complications.

Some authors [1,3] have reported that pulmonary complications are the most common type in elderly patients. This was not the case in this study as both wound and gastrointestinal complications were more common than the pulmonary type. Probably the most significant difference in specific complication rates between the young and the old involved atelectasis, which occurred three times more frequently in patients sixty years of age or over. Whether or not emphysema, chronic lung disease or a general decrease in pulmonary function accounts for this is difficult to ascertain.

When analyzing the complications one is impressed by the frequency of infectious processes which occurred postoperatively in these patients. If unexplained fevers are included as being due to some infectious process, 37 per cent of all the complications were due to infection. This does not differ significantly from the younger group of surgical patients.

Finding that the morbidity and mortality rates in patients over sixty years of age are significantly higher than in those patients under sixty years of age certainly suggests the necessity for further investigation into these problems in the elderly patient.

A rigid definition and classification of postoperative complications is needed in a study of this type. With the help of valid statistics the exact incidence of postoperative complications can be determined and technic applied toward reducing the more common complications in the elderly surgical patient.

SUMMARY

1. A review of 723 operations performed upon patients sixty years of age or over on the

general surgical service showed that 523 were major operations, of which 35 per cent were followed by one or more postoperative complications. This compared to a 23 per cent complication rate in patients under sixty years of age for the same time period. The complication rate for minor surgery in the elderly patients was 11 per cent compared to 4 per cent in the younger patients.

2. The mortality rate following major surgery in the patients sixty years of age and over was 8.5 per cent compared to 4 per cent in the patients under sixty years of age. Pulmonary complications were the most frequently encountered type in those patients who died postoperatively.

3. More complications arose in the elderly male than in the elderly female patient.

4. Wound and gastrointestinal complications were the most frequent encountered.

5. Extreme obesity (30 per cent or more above ideal weight) was associated with a higher complication rate but moderately obese patients had no increase in complications.

6. Atelectasis was three times more common in elderly patients than in patients under sixty years of age.

7. The need is pointed out for more accurate recording of postoperative complications if proper steps are to be taken to reduce our current complication rate.

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Pancreatic Cystogastrostomy

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PANCREATIC pseudocysts have been treated by every method surgically possible. Success has attended all the popular methods. Ideally, a cyst is extirpated but this is rarely feasible because of the enormity of most. Drainage has taken two forms: (1) external and (2) internal.

Until recent years external drainage was the treatment utilized by most surgeons. The disability caused by prolonged drainage and frequency of secondary operations prompted the quest for other forms of treatment, namely, internal drainage.

Cysts have been anastomosed to all the nearby hollow viscera—the duodenum, jejunum and stomach.

The Roux en Y drainage utilizing the jejunum is a most popular surgical technic. It obviates the danger of material from the gastrointestinal tract entering the cyst.

FIG. 1. Plain film of the abdomen showing large mass in the left upper quadrant.

At the Veterans Administration Hospital, Huntington, West Virginia, seven patients with cysts have been operated upon in the past five years. The first three patients were treated with external drainage. All required secondary operations and a minimum time of six months for healing.

The last four patients were treated with cystogastrostomy. Postsurgical hospitalization has been brief and convalescence has been totally uneventful. The following is a case history of one of these patients.

CASE REPORT

The patient was a sixty-eight year old white man who was admitted to the hospital on February 18, 1957. He complained of a weight loss of 15 pounds and pain in the upper abdomen of three months' duration. Past history revealed that he had had a stroke in 1952 with residual right hemiparesis.

Physical examination showed a well nourished male, not acutely ill, with right hemiparesis. The only other finding was a massive globular tumor in the epigastrium.

Routine laboratory findings were normal. A plain film of the abdomen revealed a mass occupying most of the upper portion of the abdomen. (Fig. 1.) Barium studies showed the stomach to be displaced downward and to the left. (Fig. 2.) It was sausage shaped. The colon was also displaced downward. (Fig. 3.)

An exploratory laparotomy was carried out on March 4, 1957. A massive cyst of the pancreas was found emerging between the stomach and liver, obscuring the stomach. A frozen section was reported as compatible with pancreatic pseudocyst. The cyst contained approximately 3,100 cc. of brownish black fluid; it was not loculated. A cystogastrostomy was performed with the anastomosis being between the cyst and the lesser curvature of the stomach, this site being the most accessible. (Figs. 4 and 5.)

A gastrointestinal series on March 19 revealed

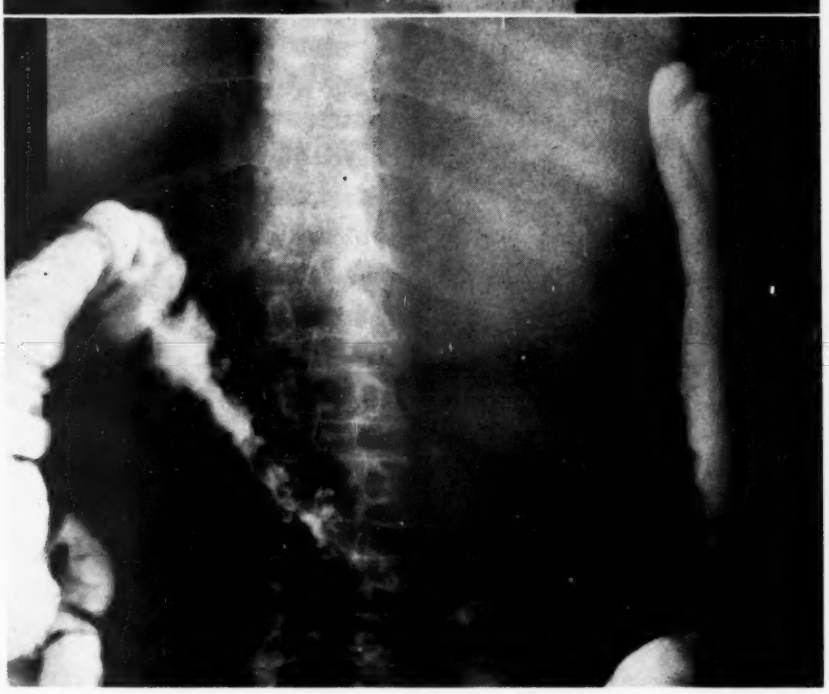

FIG. 2. Gastrointestinal series with stomach displaced downward.

FIG. 3. Barium enema showing marked displacement of colon.

the stomach to be normal in position. The anastomosis between the cyst and the stomach was patent and the cyst was outlined. (Fig. 6.) Later gastrointestinal series showed that the cyst had been obliterated and the site of anastomosis was no longer discernible. (Fig. 7.) The patient has remained totally asymptomatic.

SUMMARY

Cystogastrostomy is anatomically an ideal procedure for drainage of pancreatic pseudocysts. The stomach represents one wall of all cysts. As such the cyst can be thoroughly explored through a surgical opening into it. A

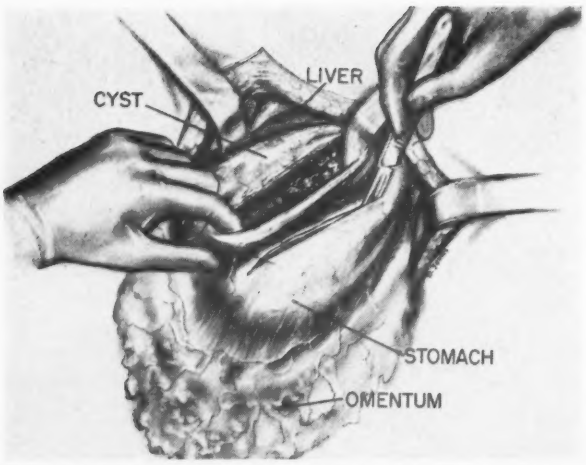

FIG. 4. Drawing illustrating location of anastomosis.

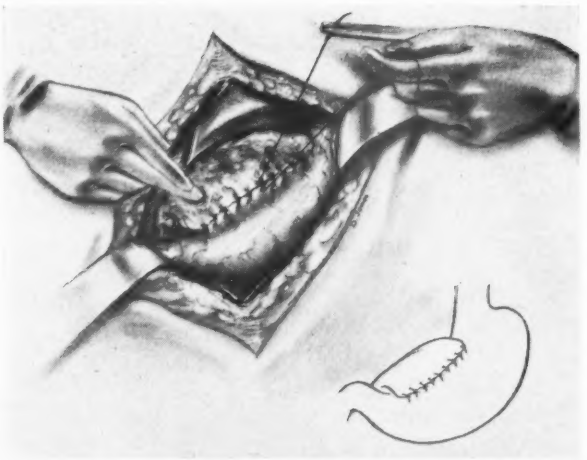

FIG. 5. Drawing of completed anastomosis.

FIG. 6. Postoperative gastrointestinal series revealing normal position of stomach and outlining remaining cyst space.

FIG. 7. Final gastrointestinal series showing cyst space obliterated and stomach normal.

comparable opening into the adherent stomach permits easy anastomosis.

Physiologically, the contents drain into the gastrointestinal tract, thus preventing the loss of considerable pancreatic juice. Fears of abscess from food lodging in the cyst have not materialized in our four cases. The cyst space has obliterated rapidly.

Finally, this procedure does not interrupt continuity of the gastrointestinal tract. The procedure is carried out in the upper portion of the abdomen, thereby lessening the possibility of postoperative adhesions.

There has been no mortality and minimal morbidity in the cases handled by this procedure. No recurrences have been noted.

Cranial Reconstruction with Ethylenediamine-Treated Bone

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From the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland and The Neurological Institute and The New York Orthopedic Hospital, Columbia Presbyterian Medical Center, New York. This investigation was supported in part by research grant No. B-1372 from the National Institute of Neurological Diseases and Blindness, Public Health Service.

BOTH biological and non-biological materials have been used in the repair of cranial osseous defects. Biological substances have included cartilage and bone of autogenous, homologous or heterologous origin; non-biological substances most commonly have been either metals or plastics [*11*]. With the belief that the repair of tissue defects is best achieved by biological replacement, this investigation was undertaken to evaluate a bone derivative, ethylenediamine-treated bone, for the repair of cranial defects.

The development of ED-treated bone was based on the hypothesis that non-acceptance of bone grafts is due to the response evoked by constituents contained in the organic fraction, i.e., proteins, fats, mucopolysaccharides, etc. [*8*]. Bone made "anorganic" by extraction with ethylenediamine, a powerful organic solvent, is devoid theoretically of antigenicity, and should therefore provide acceptability regardless of species source, be it of autogenous, homologous or heterologous origin [*4*].

The supply of ED-treated bone is limitless since osseous sources anywhere in the animal kingdom may be utilized. In addition, it is inexpensive to prepare, it may be stored indefinitely without special attention to sepsis as it is sterilized by routine autoclaving before use, and it is rapidly and readily fitted to the defect by carving with a scalpel at surgery.

METHODS

Twenty-eight adult mongrel dogs weighing between 10.0 and 24.4 kg. and unselected as to age and sex were used in this investigation. They were divided into four groups of seven animals each. The dogs in group I served as controls in which defects were created by craniotomy, and repair was effected with autogenous untreated bone grafts. The dogs in group II received autogenous ethylenediamine-treated bone grafts. Those in group III received homologous canine ethylenediamine-treated bone. The dogs in group IV were repaired with grafts of heterologous sheep ethylenediamine-treated bone.

All animals were given 600,000 units of long acting benzathine G penicillin prior to surgery. The dogs were anesthetized with intravenously administered pentobarbital sodium, 30 mg./kg. They were intubed, attached to an automatic positive-negative pressure closed system respirator, and ventilated with 100 per cent oxygen. A coronal scalp incision was made with the dogs in the prone position. The temporal-masseter muscles were reflected subperiosteally exposing the top of the calvarium down to the temporal fossae bilaterally. The largest craniotomy possible was effected, usually using 4 bur holes united by Gigli saw cuts. Bone bleeding was controlled with Gelfoam® when necessary, not bone wax.

In group I, the untreated bone flap was immediately replaced to serve as an autogenous control. In group II, the bone was removed and treated with ethylenediamine. The autogenous treated skull was reinserted forty-eight hours later at a second operation. (Fig. 1.) In the interim, the incision was closed in layers over steel screening for temporary protection. In

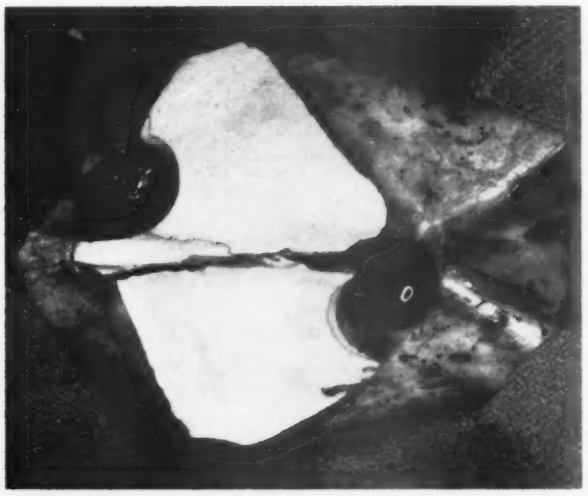

FIG. 1. Autogenous ethylenediamine-treated skull graft. The bone had been removed from this animal forty-eight hours previously, had been extracted with ethylenediamine, and is shown at the time of implantation.

group III, the defect was filled immediately with canine homologous skull which had been extracted with ethylenediamine. This bone had been prepared and stored previous to surgery and was sterilized by autoclaving at the time of its use. A template of the defect was made with a large cottonoid from which the bone graft was fashioned at the operating table by carving with a scalpel. In group IV, the same procedure was followed using heterologous treated cranium from sheep as the graft material. All grafts were free, the only fixation being the presence of imbricated temporal fascia over the top of the graft at midline. The remainder of the incision was closed in layers.

Postoperatively, the animals were observed for any local or systemic reactions, including abnormal activity of the nervous system such as seizures. No anticonvulsants were administered; the only medication given was a weekly injection intraperitoneally of 1 ml. of a saturated solution of alizarin red S which is a vital stain for new bone. X-ray films of the skull were taken every four weeks and immediately *ante mortem*. One animal of each group was sacrificed at intervals of three, four and a half, six, seven and a half, nine, ten and a half and twelve months by intracardiac perfusion of formalin. The tops of the skulls were removed *en bloc* and x-rayed and photographed with conventional and ultraviolet light. The specimens were examined grossly and sections were taken for histological study and microradiography [6]. The brains were examined grossly and microscopically for any untoward changes.

CRITERIA FOR EVALUATION

Graft Status. Reactive bone: New osseous tissue (callus) produced by the host in response to local trauma, originates from periosteum (15 per cent), raw bone ends (15 per cent), and endosteum (60 per cent) [7]. Grades are classified as: poor—trace of host response; fair—minimal host response with extension to the graft; good—extensive host response with invasion of the graft; excellent—extensive host response with diffuse involvement of the graft.

Revascularization: This is invasion of the interstices of the bone by mesenchymal elements with formation of new vascular channels. Grades are classified as: poor—endothelialization of the periphery of the graft; fair—endothelialization of the graft to a moderate degree with some capillary formation; good—vascularization of the interstices of the graft; excellent—extensive influx of mesenchymal elements, arteries, veins, lymphatics, into the interstices of the graft.

Incorporation: This is the integration of the implant by the host in such a manner and to such a degree as to produce union and solidarity of the two parts. Grades are classified as: poor—no union; fair—trace of union; good—complete union; excellent—union and solidarity.

Remodelling: This is the dynamic process by which bone is resorbed or absorbed and replaced by new bone (accretion, "creeping substitution," appositional growth). Grades are classified as: poor—slight degree of perivascular new bone at the periphery; fair—deposition of new bone; good—replacement of graft by new bone, up to an estimated 50 per cent; excellent—replacement of graft by new bone, and by marrow, more than 50 per cent, with the formation of osteons 4 to 5 lamellas in thickness. An osteon is a Haversian system in which may be seen vascular channels surrounded by two or more lamellas of new bone.

Radiographic Criteria. Fusion: This is union about the periphery at the junction of the graft and host classified according to percentage of the periphery united.

Opacity: This is the state of radiolucency. Grades are classified as: increased ↑, decreased ↓, or unchanged.

Fit: This is the anatomical apposition and alignment of the graft. Grades are classified as: poor—lack of apposition through widening of the kerf or displacement of the graft; fair—partial apposition and no displacement; good—

TABLE I

GROUP I—AUTOGENOUS UNTREATED FRESH SKULL GRAFTS

Dog (No.)	Age of Graft (mo.)	Size of Graft (sq. cm.)	Status of Graft				Convulsions	Local Changes	Systemic Changes	Radiographs				Remarks
			Reactive Bone	Revascularization	Incorporation	Remodelling				Fusion (%)	Opacity	Porosity	Fit	
3172	3	18.0	Good	Good	Excellent	Good	0	0	0	55	—	—	Fair	Slight bridging at 12 wk.
3387	4½	11.1	Good	Good	Good	Good	0	0	0	70	—	—	Good	Bridging at 8 wk.
3409	6	11.2	Good	Good	Good	Good	0	0	0	60	—	—	Excellent	Bridging at 8 wk.
3279	7½	18.2	Excellent	Excellent	Excellent	Good	0	0	0	65	—	—	Good	Bridging at 8 wk.
3345	9	19.8	Excellent	Excellent	Good	Excellent	0	0	0	80	—	—	Excellent	Bridging at 4 wk.
3428	10½	19.1	Excellent	Excellent	Excellent	Excellent	0	0	0	65	—	—	Excellent	Bridging at 4 wk.
3317	12	13.9	Excellent	Excellent	Excellent	Excellent	0	0	0	65	—	—	Good	Bridging at 4 wk.

NOTE: — = unchanged.

TABLE II

GROUP II—AUTOGENOUS ETHYLENEDIAMINE TREATED SKULL GRAFTS

Dog (No.)	Age of Graft (mo.)	Size of Graft (sq. cm.)	Status of Graft				Convulsions	Local Changes	Systemic Changes	Radiographs				Remarks
			Reactive Bone	Revascularization	Incorporation	Remodelling				Fusion (%)	Opacity	Porosity	Fit	
3542	3	11.7	Poor	Poor	Poor	Poor	0	+	0	45	↑	—	Poor	Bridging at 4 wk., partial encapsulation
3532	4½	14.5	Poor	Poor	Poor	Poor	0	+	0	50	—	—	Poor	Infected with silk sinus; partial encapsulation—new good bone in base
3442	6	13.5	Excellent	Good	Good	Good	0	+	0	60	↑	↓	Excellent	Bridging at 8 wk, new good bone in base, fibrosis, giant cells, encapsulated, questionable infection
3311	7½	16.8	Good	Fair	Fair	Excellent	0	0	0	40	—	↑	Fair	Bridging at 8 wk., fragmented with solid union between each piece
3324	9	12.6	Good	Fair	Poor	Poor	0	+	0	40	↑	↑	Fair	Infected—silk sinus, new bone in base
3579*	10½	....	.....	.....	.....	.....	0	..	..	..	—	—	Excellent	Bridging at 8 wk.
3351	12	18.2	Good	Good	Good	Excellent	0	0	0	55	—	—	Fair	Bridging at 8 wk.

NOTE: ↑ = increased
↓ = decreased
— = unchanged

* Dog observed for nine months, then stolen from kennel. Final evaluation not obtainable.

partial apposition plus narrowing of the kerf; excellent—complete or almost complete obliteration of the kerf and anatomical reapproximation.

RESULTS

Group I—Autogenous Fresh Untreated Skull Grafts. The grafts in this group ranged in size from 11.1 to 19.8 sq. cm. (Table 1.) In general, autogenous bone provided the best graft material from among the groups tested. There was radiographic evidence of bony bridging as early as four weeks following implantation. No changes in opacity or porosity were found. The grafts were fused at the periphery through 55 to 80 per cent of their circumference. (Fig. 2.) No systemic reactions were seen subsequent to grafting nor were convulsions observed. At autopsy, gross examination disclosed sparse staining by alizarin red S, and this primarily at the periphery of the graft. The radiographic evidence of fusion was confirmed. (Fig. 3.)

Microscopically, extensive host response with invasion of the graft by reactive new bone was noted. The interstices of the grafts were well

FIG. 2. Autogenous, fresh, untreated skull graft seen at time of sacrifice three months after implantation.

invaded by new vascular channels. Bony apposition was found about most of the periphery between the host and the graft. Remodelling of the grafts with deposition of perivascular new bone was present early and increased noticeably between seven and a half and nine months. It is noteworthy that areas of devitalized bone were observed throughout the grafts, except for an area 30 to 60 microns thick at the surface where the cells had apparently remained viable subsequent to reimplantation. Within these segments of devitalized bone, the macrocanalicular spaces were found to have been revascularized and osteons in various stages of development were observed. (Fig. 4.) These areas of living bone were differentiated sharply from adjacent dead

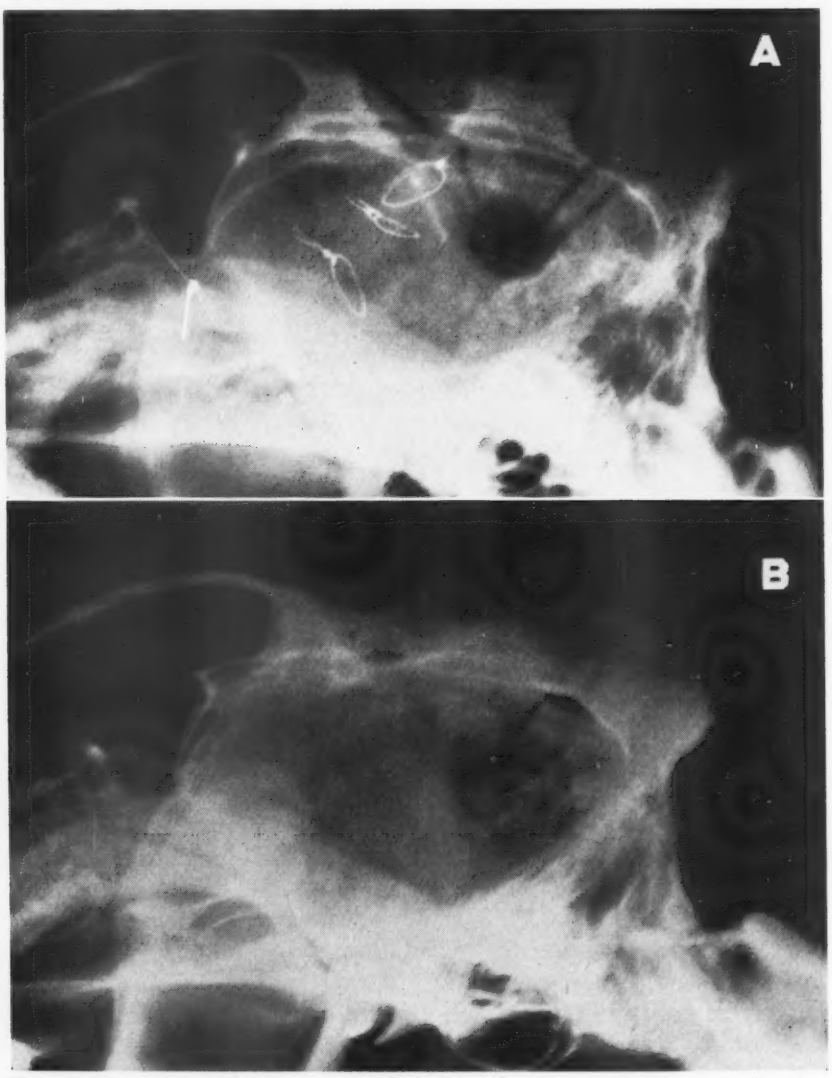

FIG. 3. Autogenous, fresh, untreated skull graft. A, roentgenogram taken immediately postoperatively and B, at the time of sacrifice ten and a half months later.

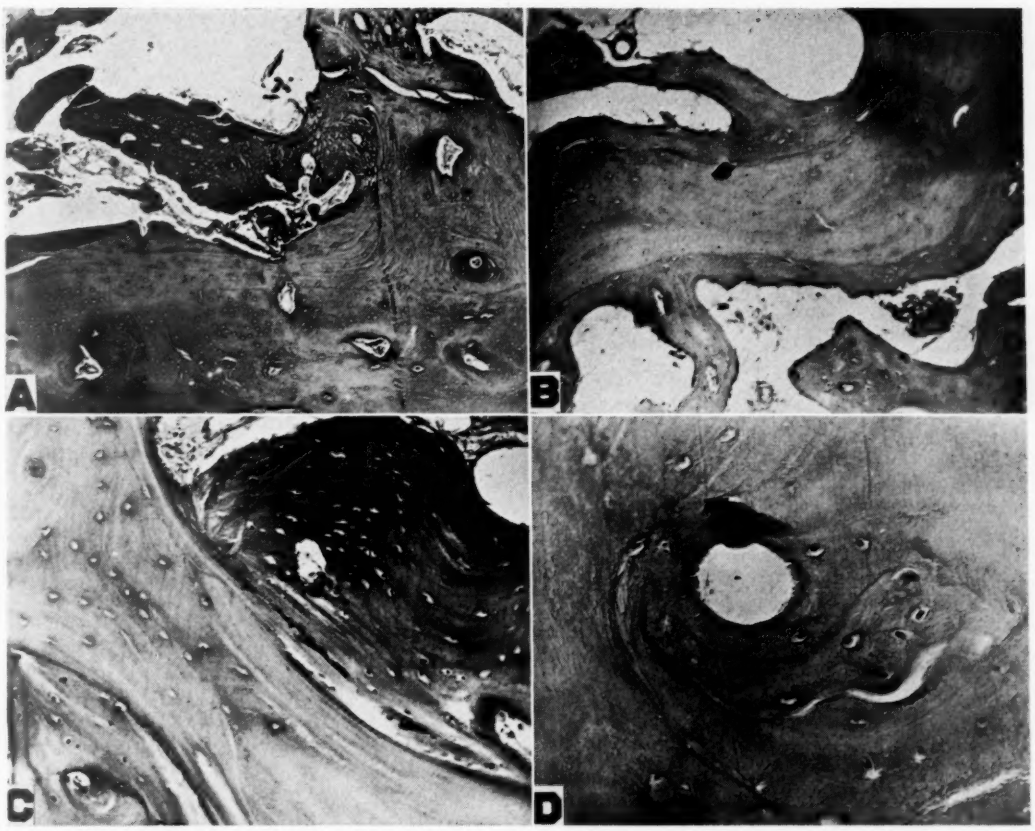

FIG. 4. Autogenous, fresh, untreated skull graft, twelve months of age. Section through center of graft. Hematoxylin-eosin stain. A, vital bone (upper left) is distinguished from non-vital bone (lower right) by presence of osteocytes in lacunas and by darker staining. Original magnification, × 40. B, junctional area, non-vital bone (center) incorporated in new bone formation, note lamination. Original magnification, × 40. C, periphery of graft, vital bone and marrow (upper right and lower left) is easily distinguished from non-vital autograft, (center). Original magnification, × 120. D, new osteon surrounded by non-vital graft. Original magnification, × 240.

bone, the dead bone being distinguishable by its paler staining characteristics and lacunas devoid of osteocytes.

Group II—Autogenous Ethylenediamine-Treated Skull Grafts. The grafts in this group of animals ranged in size from 11.7 to 18.2 sq. cm. (Table II.) This group produced the poorest results in this study. Three of the seven dogs in this series became infected. It was believed that the inordinate number of infections was due to the additional exposure and risk incurred at the second operation for the replacement of the treated graft. (Fig. 1.) The infections induced local changes in the form of thickening of the dura mater and partial encapsulation of the graft; however, no untoward effects upon the nervous system were observed.

Radiographically, bridging again was seen as early as four weeks. Fusion at the periphery was much less extensive in the infected animals and changes in opacity and porosity were found. The anatomical fits were graded as poor to fair, except in two instances. This was attributed to a small amount of shrinkage which occurred in the extraction of the bone with ethylenediamine. The shrinkage produced a widened kerf and less perfect approximation of graft to host. This factor plus infection resulted in conditions disadvantageous for the acceptance of the implants.

Histologically, excessive fibrous tissue was present in many of the grafts. Where this had occurred no new bone formation was found. The isolated non-vital implants were gradually undergoing resorption and replacement by avascular fibrous sheets of tissue. Likewise, new bone was not found in areas which showed polymorphonuclear and lymphocytic infiltration. Instead, dense fibrous tissue formed the parenchyma of the reactive elements which surrounded the grafts. However, in adjacent

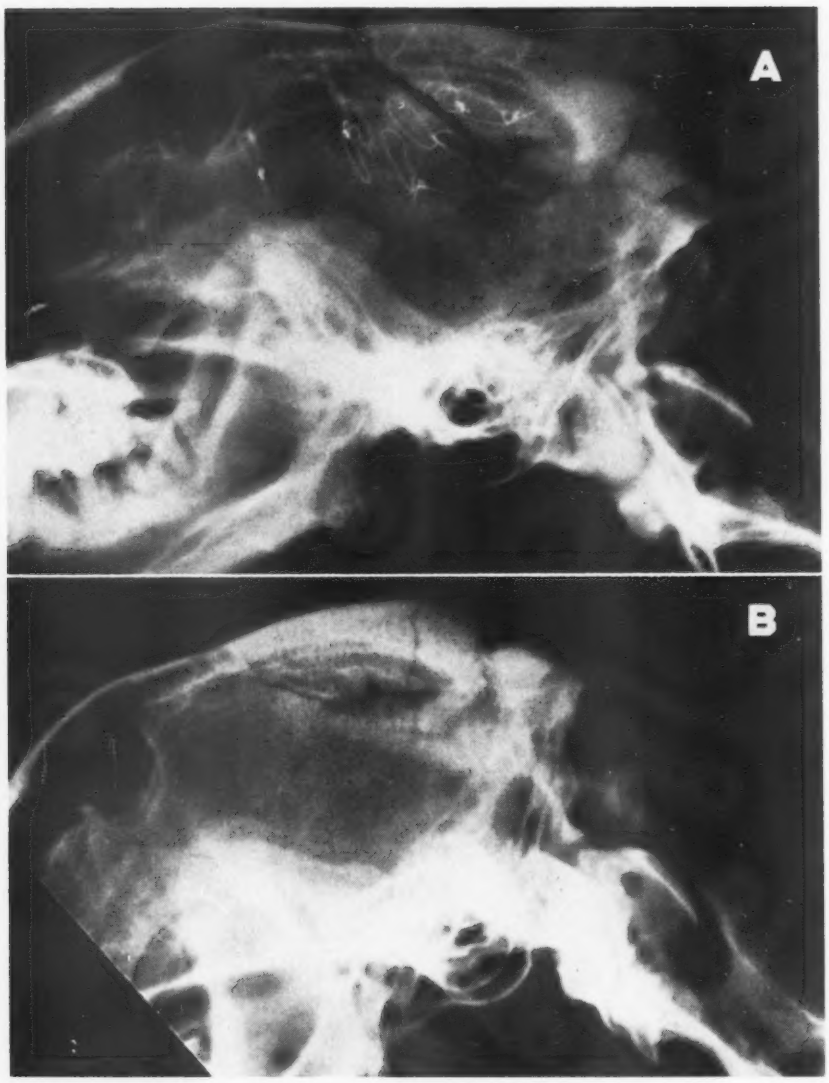

FIG. 5. Homologous, ethylenediamine-treated skull graft. A, roentgenogram taken immediately postoperatively and B, at the time of sacrifice six months later.

areas not so involved, healthy new bone was seen which did not differ in appearance from the bone seen in uninfected animals. Because of these factors, ratings in this series were low in regard to reactive bone formation, revascularization, incorporation and remodelling.

Group III—Homologous Ethylenediamine-Treated Grafts. The grafts in this group ranged in size from 14.1 to 24.6 sq. cm. (Table III.) The results of the homologous ethylenediamine-treated implants were better than the autogenous treated bone series but not as good as the heterologous ethylenediamine-treated bone. The anatomical fit of these grafts was fair to excellent. Radiographically, bone bridging occurred as early as four weeks. Fusion about the periphery was estimated at 50 to 75 per cent of the circumference, except for the three-month graft (Fig. 5.) In this group, changes in opacity and porosity were seen consistently. The porosity always increased. In all but one instance (dog No. 3531), histological examination indicated that these changes were *not* evidence of an undesirable tissue response. On the contrary, it appeared that these changes were a result of a physiological process leading to alteration of the inorganic matrix of the graft, i.e., remodelling. With increasing age of the graft, the degree of new bone formation became progressively greater. Sections taken from grafts nine to twelve months of age showed extensive revascularization, solid incorporation

TABLE III

GROUP III—HOMOLOGOUS ETHYLENEDIAMINE-TREATED SKULL GRAFTS

Dog (No.)	Age of Graft (mo.)	Size of Graft (sq. cm.)	Status of Graft				Convulsions	Local Changes	Systemic Changes	Radiographs				Remarks
			Reactive Bone	Revascularization	Incorporation	Remodelling				Fusion (%)	Opacity	Porosity	Fit	
3050	3	16.2	Poor	Fair	Poor	Poor	0	+	0	35	—	—	Fair	Bridging at 6 wk., partially encapsulated, fibrosis, no inflammatory cells
3531	4½	14.1	Fair	Fair	Poor	Poor	0	+	0	60	—	↑	Excellent	Bridging at five wk., was reoperated upon, infected, partial capsule, good bone in base
3184	6	24.6	Fair	Fair	Fair	Poor	0	+	0	70	—	↑	Excellent	Bridging at 6 wk., neomembrane, no inflammatory cells
3450	7½	18.6	Good	Excellent	Fair	Fair	0	0	0	50	↑	↑	Fair	Bridging at 6 wk., fragmented but solid union between pieces
3356	9	17.6	Good	Excellent	Fair	Fair	0	0	0	75	↓	—	Excellent	Bridging at 12 wk, fragmented but solid union between pieces
3447	6½	19.3	Excellent	Excellent	Excellent	Good	0	0	0	75	↑	—	Excellent	Bridging at 8 wk.
3075	12	19.1	Excellent	Excellent	Excellent	Excellent	0	0	0	75	↑	↑	Excellent	Bridging at 4 wk., marrow and active hemopoiesis present

Note: ↑ = increased
↓ = decreased
— = unchanged

TABLE IV

GROUP IV—HETEROLOGOUS ETHYLENEDIAMINE-TREATED SKULL GRAFTS

Dog (No.)	Age of Graft (mo.)	Size of Graft (sq. cm.)	Status of Graft				Convulsions	Local Changes	Systemic Changes	Radiographs				Remarks
			Reactive Bone	Revascularization	Incorporation	Remodelling				Fusion (%)	Opacity	Porosity	Fit	
3439	3	14.4	Good	Good	Good	Fair	0	0	0	75	—	—	Excellent	Bridging at 4 wk.
3451	4½	11.7	Excellent	Good	Good	Good	0	0	0	75	—	—	Excellent	Bridging at 12 wk.
3348	6	12.1	Good	Good	Good	Good	0	0	0	65	—	↑	Excellent	Bridging at 4 wk.
3380	7½	22.3	Excellent	Good	Good	Excellent	0	+	0	45	↓	↑	Excellent	Bridging at 4 wk., thin capsule—no inflammatory cells
3526	9	21.2	Good	Good	Good	Excellent	0	0	0	60	↑	↑	Fair	Bridging at 4 wk., some soft tissue interposition
3393	10½	21.4	Excellent	Good	Good	Excellent	0	0	0	65	—	↑	Excellent	Bridging at 4 wk.
3216	12	17.6	Excellent	Good	Good	Excellent	0	0	0	60	↑	↑	Excellent	Bridging at 4 wk., fractured with solid union between pieces

Note: ↑ = increased
↓ = decreased
— = unchanged

of the graft, and a significant degree of remodelling. In many areas, as much as 80 per cent of the original crystalline lattice had been replaced by new bone. (Fig. 6.) Marrow with evidence of active hemopoiesis was found which was interpreted as indicating that physiological as well as mechanical restitution had occurred.

Group IV—Heterologous Ethylenediamine-Treated Grafts. Grafts in this group ranged in size from 14.4 to 22.3 sq. cm. (Table IV.) Of all the ED-treated grafts, the heterologous sheep implants were the best. Except in one case (dog No. 3526), excellent apposition and alignment were achieved. (Fig. 7.) Bridging occurred in all but one animal at four weeks. The roentgenographic estimate of fusion was 60 to 75 per

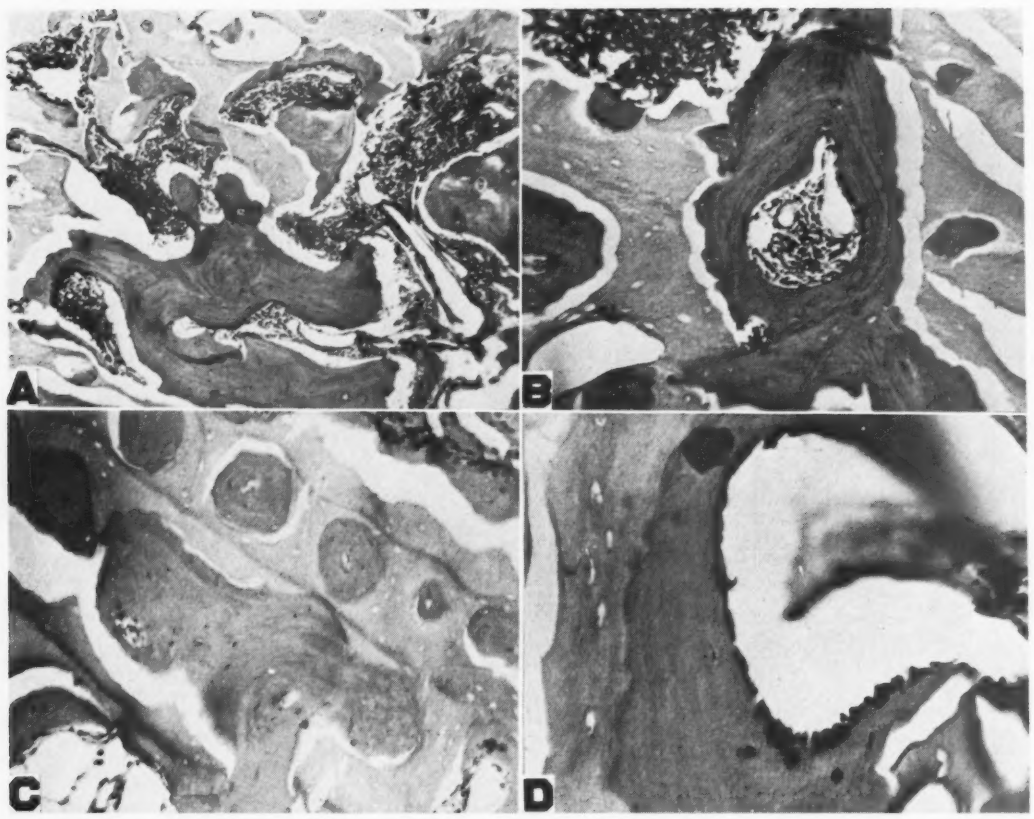

FIG. 6. Homologous ethylenediamine-treated skull graft twelve months after implantation. Section through center of graft. Masson's trichrome stain. Dark-stained tissue indicates viable bone. Acellular, pale-stained tissue indicates non-vital ED-treated bone. A, marked new bone formation and presence of hemopoietic tissue. Original magnification, × 40. B, remodelling and osteon formation. Original magnification, × 120. C, perivascular accretion of new bone. Original magnification, × 100. D, osteon, layer of osteoblasts lines inner lamella. Original magnification, × 200.

FIG. 7. Heterologous ethylenediamine-treated skull graft seen at the time of sacrifice three months after implantation.

cent except for No. 3380 (45 per cent). X-ray films taken at the time of sacrifice showed an increase in porosity of grafts more than four and a half months of age. Here too, as was seen in group III, the changes in opacity were found. Again, these radiological alterations could *not* be interpreted as being indicative of a pathological tissue response. The histological study disclosed grafts undergoing physiological remodelling. (Fig. 8.)

The postoperative clinical course of the animals in this group was uneventful. There were no abnormal neurological manifestations. The incisions healed *per primam*. At the time of sacrifice, reactive new bone as indicated by the presence of pink stained areas of alizarin red S was noted at the edge of the skull defect. Alizarin-stained areas were also found throughout the graft itself. Microscopic studies indicated that all grafts had been accepted. No evidence of foreign body reaction (giant cells, lymphcytes, etc.) was observed. The grafts were incorporated in new bone; they were revascularized and remodelled in all instances. There appeared to be a direct relationship

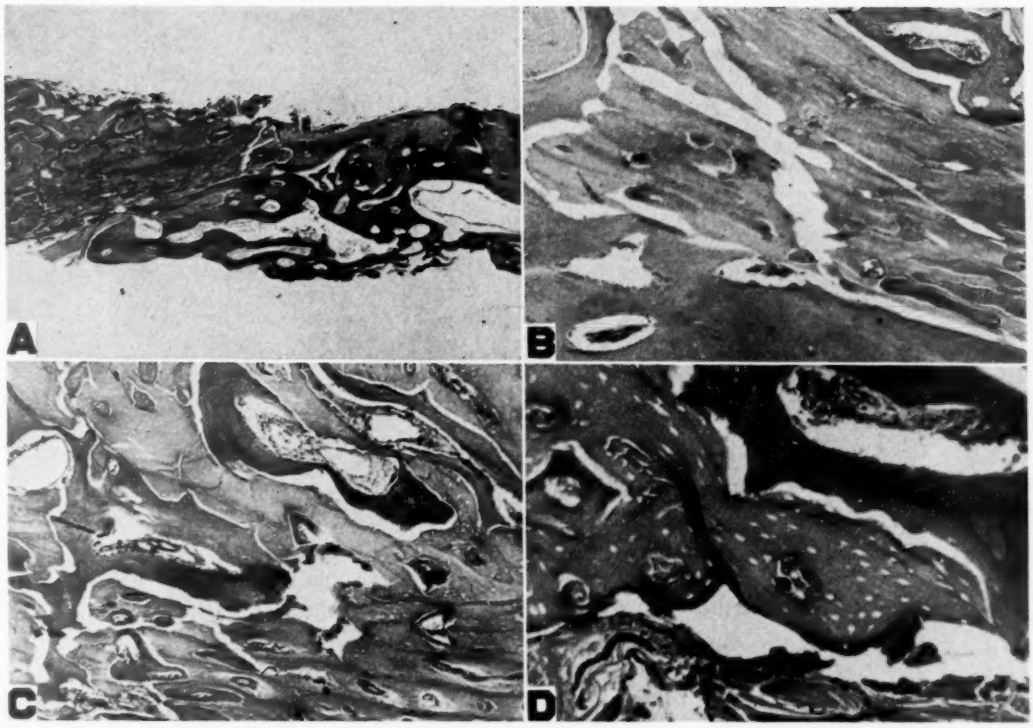

FIG. 8. Heterologous ethylenediamine-treated skull graft four and a half months of age. Hematoxylin-eosin stain. A, junction of host (right) and graft (left). Original magnification, × 10. B, junctional area. Original magnification, × 45. C, center of graft, dark staining areas surrounding blood vessels represent revascularization with new bone deposition, pale staining areas with empty lacunas represent ethylenediamine-treated bone. Original magnification, × 45. D, remodelling with appositional new bone growth several lamellas in thickness (upper right), pale staining bone with empty lacunas (center) is ED bone residuum. Scattered islands of darker staining material represent endothelialization and perivascular new bone formation. Original magnification, × 120.

between the age of the graft and the degree of remodelling. During the first seven and a half months approximately 50 per cent of the graft had been replaced by new bone. Thereafter, the rate of new bone deposition appeared to have decreased, reaching an estimated level of 75 per cent at twelve months, the longest period of observation in this study.

Comparative Evaluation of Groups I to IV. The autogenous, fresh, untreated skull provided the most acceptable functional graft. Thereafter, the order of acceptance was heterologous ED-treated skull, homologous ED-treated skull, and autogenous ED-treated skull. The rates of osteogenesis among the groups tested did not appear to be appreciably different, except for the autogenous ED-treated grafts. In this group, the rate was decreased. However, mechanical not biological factors were thought to account for the low rating of the autogenous ED-treated grafts. That is, because of the shrinkage of the graft, resulting from processing, soft tissue interposition occurred in the widened kerfs and good anatomical apposition was prevented. Without good apposition, revascularization and the ensuing sequence of events were not possible; hence, a poor result was inevitable. Since this was autogenous bone, an antigenic response is excluded. The precedence of heterologous over homologous bone is unexplained.

Physically, the autogenous fresh bone was hard and resistant to forces applied to it. No fractures occurred in this group. By contrast, the ED-treated bone was brittle and fractured easily, especially in the early post-grafting stages. It was usual, however, to find that the fractured segments were united solidly by new bone at the time of sacrifice. Protective function was being served and the mechanical integrity of the graft was good. Bony deformity did not occur. This was somewhat surprising in view of the trauma to which the grafts were subjected. In the dog, the temporal-masseter muscles almost completely cover the top of the calvarium. In the grafted dogs, these muscles were imbricated over the implants. Thus, postoperatively, with each motion of the jaws the

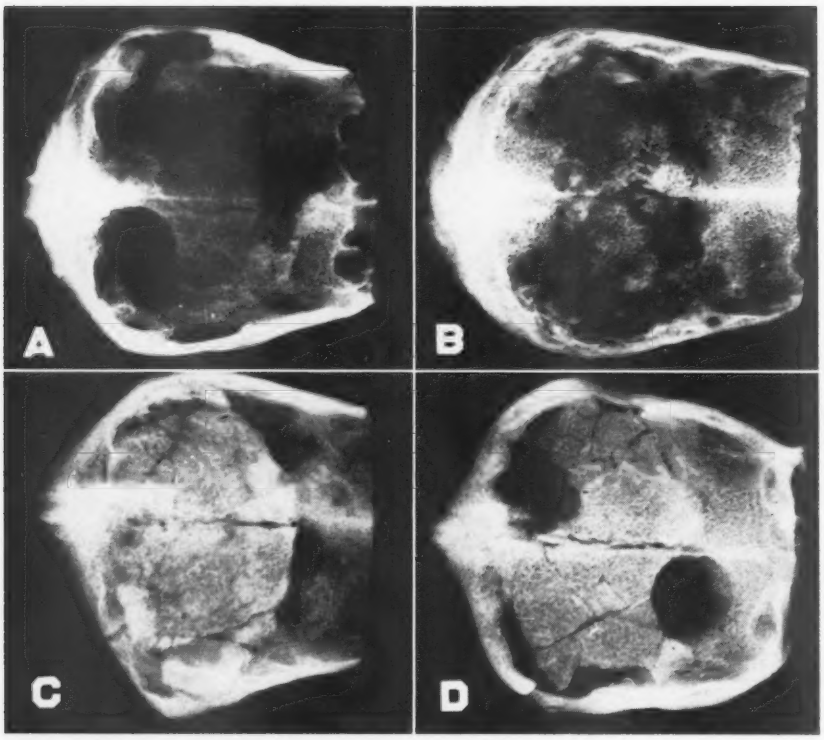

FIG. 9. Roentgenological comparison of the four groups of grafts. A, fresh, untreated autograft at seven and a half months. B, ED-treated heterograft at six months. C, ED-treated homograft at ten and a half months. D, ED-treated autograft at twelve months.

animal exerted extremes of pressure upon the graft. It was no wonder then, that ED-treated grafts fractured. However, despite this factor union occurred and a good mechanical result was found.

Radiographically, the fresh autografts exhibited no changes in opacity or porosity. Fusion about the periphery occurred regularly. (Fig. 9A.) By contrast, the ED-treated grafts did show alterations of both these properties. Porosity increased usually (except in one instance) where infection had occurred. When changes in opacity occurred, the change was inconsistent, either increasing or decreasing. The six-month heterograft (Fig. 9B) demonstrated increased porosity without a change in opacity. The ten and a half month homograft (Fig. 9C) showed increased opacity without an alteration in porosity. The twelve-month ED-treated autograft (Fig. 9D) exhibited no changes. It is to be re-emphasized that these alterations seen on roentgenograms reflected only physiological processing and replacement of the graft by the host, not a pathological reaction.

There were no instances of convulsions or other abnormal nervous system manifestations. Systemic reactions were not observed. Local changes did occur, in some cases, primarily in response to infections. However, these were surface phenomena and were restricted to the epidural space and integument.

COMMENTS

The bone in this study was prepared by the method of Williams and Irvine [*15*] as modified by Losee and Hurley [*8*]. In this process, the organic matrix of bone is removed leaving behind the inorganic structure. Extraction of the organic constituents of bone is accomplished in a modified Soxhlet distillation apparatus by the action of a strong organic solvent, ethylenediamine. The concept of modifying the organic matrix of bone is not a new one. Orell, in 1937, published the results of experiments in which ox bone was freed of periosteum, endosteum and of all the other elements of the connective tissue series by a process of maceration [*10*]. The resulting product was called "os purum." The preparation of the product was described as a complicated, wearisome process to be carried out only by a specially trained and quali-

fied chemist. Maatz and Bauermeister have also reported the experimental and clinical use of macerated bone prepared by such a complex and expensive procedure [9]. By contrast, ethylenediamine-treated bone can be produced in any laboratory by a simple, inexpensive method. In addition, it has other commendable attributes.

Because of the removal of its organic components, theoretically, ED-treated bone is incapable of evoking antigenic activity. The source of bone, is therefore limitless as bone may be obtained from any osseous origin regardless of species. If large scale use of bone for grafting should become necessary, as in a national emergency, this advantage would be great. The bone to be obtained for processing need not be taken from sterile sources as is required by other forms such as freeze-dried bone, cultured bone, etc. [1,2,5,14]. Ethylenediamin-treated bone is sterilized by routine autoclaving technics and sterilization may be repeated *ad infinitum* [12]. While awaiting use, ED-treated bone is stored on the shelf without sterile precautions or special care for indefinite periods. When ready for use, ED-treated bone may be measured and fitted readily to the defect by simply carving with a scalpel much in the manner that balsa wood is fashioned. Thus, oddly shaped defects may be repaired with ease.

Although the advantages are many, some disadvantages do exist. Ethylenediamine-treated bone is brittle. It withstands compression well, but not shearing or torsion. It is inelastic. However, within three months of its implantation in the skull, ED-treated bone assumes, to a considerable degree, the characteristics of normal bone. Thereafter, the replacement process continues progressively at a slowed rate. In the present study, twelve months was the longest period of observation. During this time, none of the specimens were replaced completely with new bone; however, at the end of this period the process appeared to be well advanced. It is believed that eventually total replacement would have occurred, but how long this would have taken is not known.

Practically speaking, the fresh graft must still be classified as the best because of the strength which it provides during the early postgrafting phase. Since ED-treated bone depends upon replacment by the host for restoration of its integrity, it does not offer the mechanical protection that fresh bone does during the early replacement period. However, physiologically and from an investigative viewpoint, ED-treated bone is the more interesting and, perhaps, eventually the more functional graft. Such functional ability is highlighted by the presence of marrow spaces with active hemopoiesis observed in some of the ED-treated grafts in this study. It is possible that ED-treated bone is replaced finally, producing a result which could truly be called cranial reconstruction. Complete replacement has not been observed yet, since it appears that this process takes longer to complete than the twelve month observation period utilized in this investigation.

In the paragraph in which the comparative evaluation of these grafts is discussed, the statement is made that autogenous fresh skull provided the most acceptable functional graft. By functional we mean to indicate that mechanical protection was afforded with integrity of the properties of normal bone. However, this statement requires some qualification. It is true that the fresh bone appeared to have lost none of its normal properties during the grafting procedure. It is also true that fusion about the periphery occurred throughout a large extent of the circumference of the graft. These two factors prompted the use of the phrase, most acceptable graft. However, despite the fact that the autogenous fresh graft was lifted from its bony bed only ten to fifteen minutes before reimplantation, a high degree of devitalization did occur. At autopsy, even twelve months after grafting, multiple small areas amounting to a sizeable percentage of the total graft volume were found. Within these dead segments, revascularization and remodelling were proceeding at a rate approximately that observed in the equivalent ED-treated grafts. Proportionately, however, the ED-treated bone evinced much greater dynamic activity and so intense was this reaction that changes in radiological properties occurred in the form of alterations of porosity and density. Such intense activity was not seen with the fresh autograft.

This study was undertaken as an investigation of bone physiology as well as an attempt to explore experimentally the possible advantages of ED-treated bone for cranioplastic repair. The former subject has been presented already, it is not the purpose of this report to consider the clinical aspects of cranioplasty.

TABLE V

COMPARISON OF COMMONLY USED CRANIOPLASTIC MATERIALS WITH ETHYLENEDIAMINE-TREATED BONE

Data	Bone	Cartilage	Metals	Plastics	ED-Treated Bone
Availability	Autogenous: limited Homologous: limited Heterologous: unlimited	Autogenous: limited Homologous: limited Heterologous: unlimited	Unlimited	Unlimited	Unlimited
Expense	.....	.....	Expensive	Inexpensive	Inexpensive
Preparation	Autogenous: 2nd operation, 2nd site Homologous: bank-complex Heterologous: bank or cultured-complex	2nd operation, 2nd site or bank-complex	Simple to complex; may need mold	Simple to complex; may need mold	Simple
Storage and sterilization	Sterile at operation or autopsy for bank-special complex care	Sterile at operation or autopsy for bank-special complex care	Shelf, autoclave or germicide	Shelf, supplied in sterile packs	Shelf, autoclave
Insertion	Difficult, if not autogenous flap	Easy if source accessible	Easy if defect small; difficult if mold needed	Easy if defect small; difficult if mold needed	Easy, carved with scalpel
Strength	Good to excellent	Poor to fair	Good; may deform with trauma	Good, fractures easily	Poor early, gains with time until normal bone is approximated
Dead space	No	No	Yes	No	No
X-ray transmission	Yes	Yes	No	Yes	Yes
Temperature conduction	.....	.....	Extreme	Poor	.....
Growth	Yes	Yes	No	No	Yes
Psychological effect	Good	Questionable	Poor to good	Poor to good	Good
Acceptance, reactivity	Autogenous: good to excellent Homologous: fair to good Heterologous: poor to fair, foreign body reaction	Resorbed, no bone	5 per cent rejection, inertness questionable, encapsulation	Rejection rate unknown, inertness questionable, encapsulation	Good to excellent, no foreign body reaction
Fate	Partial replacement	Replaced by fibrous tissue	Unchanged	Unchanged	Replaced by host with new living bone

This is discussed thoroughly in the publications of Grant and Norcross [3], Woolf and Walker [16], Reeves in his monograph entitled "Cranioplasty" [11], and Spence [13]. Their composite opinions include the following indications for cranioplasty: the repair of defects caused by trauma to the head, removal of tumor, removal of infected bone, and surgical decompression, especially when the defects are associated with severe headache, epilepsy, painful pulsations, fear of injury or an unsightly cosmetic appearance. The attributes of currently used materials are listed in Table v and are compared with ED-treated bone.

The advantages and disadvantages of ED-treated bone are recognized. The results of this study have been sufficiently rewarding to justify limited experimental usage in man. Such a project is in progress at present and will form the subject of a future report.

SUMMARY AND CONCLUSIONS

Ethylenediamine-treated bone grafts of autogenous, homologous and heterologous origin were implanted into dog skulls and were compared with grafts of fresh, autogenous, untreated bone. The order of biological acceptance of the grafts was: fresh, autogenous, untreated skull; heterologous, ED-treated skull; homologous, ED-treated skull; and autogenous, ED-treated skull. No untoward tissue or clinical responses were observed. The ED-treated grafts were revascularized, remodelled, and incorporated progressively with time so that solid union of the graft to host was achieved.

It was concluded that ethylenediamine-treated bone, regardless of species source, was an effective graft.

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ADDENDUM

Ethylenediamine-treated bone has been implanted into more than 100 neurosurgical patients. The size of the grafts ranges from that used to fill in $\frac{5}{8}$ inch diameter bur holes to replacement of cranial defects measuring up to 135 sq. cm. No untoward reactions have been seen and no grafts have been rejected. The longest follow-up period is now two years.

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Segmental Dilatation of the Colon

A NEW ENTITY

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THREE patients have been observed with unusual segmental dilatation of the colon which does not fit into any previously described category. All three patients had persistent symptoms since infancy; consequently it is assumed that these conditions represent congenital malformations. Each patient was referred to our hospital with the diagnosis of Hirschsprung's disease (congenital aganglionic megacolon), and in general the history was consistent with the diagnosis. One child had a fusiform dilatation of the sigmoid colon which made it indistinguishable from aganglionic megacolon. In the second child the lesion was in the proximal transverse colon and was thought to represent dilatation proximal to a long aganglionic segment extending from the anus to the mid-transverse colon. In the young adult the dilatation involved the entire sigmoid colon.

CASE REPORTS

CASE I. N. C., a six month old white female child born of a full term pregnancy, was hospitalized in 1953 because of repeated bouts of vomiting, mucous and blood-containing stools and abdominal distention with a palpable abdominal mass. A barium enema examination made shortly after birth revealed a narrowed bowel from the anus to the mid-transverse colon, and a large fusiform dilatation of the right transverse colon. A second examination at three months of age exhibited similar findings and was interpreted as stenosis of the transverse colon due to congenital aganglionic megacolon, or possibly a duplication of the transverse colon.

Examination on admission showed a healthy, well developed and well nourished six months old infant with moderate anemia. The abdomen was distended and contained masses in the right side which were considered to be fecal impactions. There was a tight anal sphincter with an empty rectal ampulla. Stools contained occult blood. Barium enema revealed narrowing of the transverse colon with dilatation of the hepatic flexure, consistent with the diagnosis of Hirschsprung's disease. (Fig. 1.) Due to the unusual length of the narrow segment it was decided that rectal biopsy would be appropriate. As ganglion cells were present, the most likely diagnosis was thought to be duplication of the proximal transverse colon. Laparotomy revealed a large fusiform dilatation of the proximal transverse colon, measuring 8 cm. in length and 10 cm. in diameter. (Fig. 2.) There was obvious hypertrophy of the muscularis, and the vascular branches to this segment were unusually dilated and tortuous. The ascending colon was only moderately dilated; the colon distal to the lesion was small and somewhat atrophic. There was some angulation at the junctions of the bowel with this lesion. Rapid section examinations were made and ganglion cells proved to be present in the lesion and also in the colon proximal and distal to it. Segmental, aseptic resection with end-to-end anastomosis utilizing one layer of silk sutures was performed. The postoperative course was uneventful, and the infant was discharged from the hospital on the eighth postoperative day. The child has been symptom-free and is now five years old. Bowel movements are normal. Barium enema shows a normal colon except for a mobile cecum. (Fig. 3.)

CASE II. D. C., a two and a half year old white female infant born of a normal full term pregnancy, was hospitalized in 1958 with the diagnosis of Hirschsprung's disease. History revealed that there were watery stools at three weeks of age and considerable abdominal distention. Frequent enemas were required until six months of age when these became ineffectual, and colonic irrigations were required to combat obstipation. Several barium examinations were performed, most of which were considered pathognomonic of Hirschsprung's disease. (Fig. 4.)

On admission the healthy appearing child had moderate abdominal distention, and several fecal

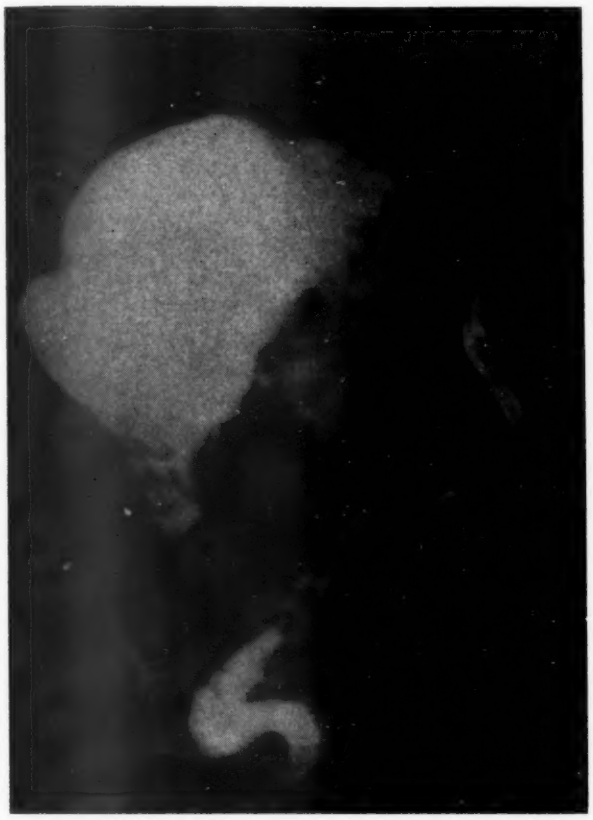

FIG. 1. Case 1. Barium enema outlining the colon. The massive fusiform dilatation of the right transverse colon is clearly outlined.

masses were palpated in the abdomen. Sphincter tone was normal; the rectal ampulla was empty. Laboratory findings were normal. While the history was consistent with a diagnosis of Hirschsprung's disease, one film taken prior to admission indicated such a massive localized dilatation of the colon that the diagnosis of Hirschsprung's disease was questioned. A barium enema performed after admission seemed pathognomonic of Hirschsprung's disease and a rectal biopsy was omitted. At laparotomy the colon was foreshortened and rotation was incomplete. The descending colon was enormously dilated in a fusiform manner with hypertrophy of the muscularis, marked dilatation and tortuosity of the vessels. This dilated segment measured 13.5 cm. by 22 cm. and tapered to the narrow segment in the lower sigmoid. The proximal colon was not remarkably dilated. This localized dilatation was much larger than in the average case of Hirschsprung's disease. (Fig. 5.) Nevertheless, abdominoperineal pull-through procedure was performed after rapid section studies demonstrated ganglion cells in the segment proximal to the fusiform dilatation. The patient did well for three days when intestinal obstruction developed. This did not subside with Miller-Abbott intubation and suction,

FIG. 2. Case 1. Drawing indicating the position and size of the segmental fusiform dilatation of the colon.

Fig. 3. Case 1. Barium enema five years after segmental resection of the fusiform dilatation of the right transverse colon. The cecum is free on a mesentery and is in the right upper quadrant.

FIG. 4. Case II. Roentgenogram of barium enema which seemed pathognomonic of Hirschsprung's disease.

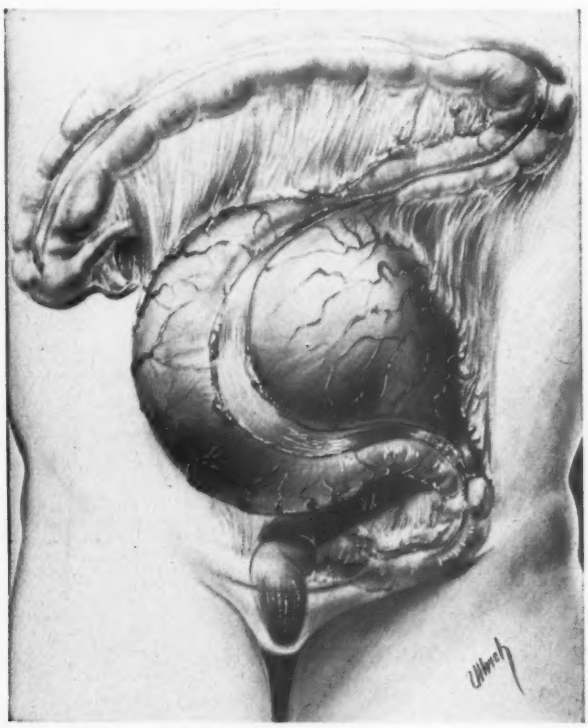

FIG. 5. Case II. Drawing indicating the position and size of the sigmoid fusiform dilatation.

and it was necessary to relieve it surgically on the fifth postoperative day. Microscopic studies revealed the presence of ganglion cells throughout the entire length of the resected specimen.

CASE III. B. C., a twenty-two year old white man, was hospitalized in 1956. The diagnosis of Hirschsprung's disease had been made by barium enema examination three months previously at another hospital. There was a history of constipation during the first weeks of life with some subsidence of these symptoms followed by increasingly severe gaseous distention, abdominal discomfort, epigastric fullness, bouts of diarrhea lasting one or two days and passage of large quantities of flatus. As a rule, bowel habits were considered fairly normal by the patient, but he did have episodes of constipation lasting four or five days.

Examination on admission showed a well developed, white male of twenty-two years, with abdominal distention and tenderness in both lower abdominal quadrants. Rectal sphincter tone was normal, and the ampulla was empty. Laboratory data were normal. Barium enema studies revealed marked elongation and widening of the sigmoid colon with its upper margin at the level of the diaphragm, persistent and slightly narrowed areas at the level of the rectosigmoid and normal caliber of the descending colon. Postevacuation studies showed satisfactory emptying of the sigmoid but persistent retention of gas with dilatation of this segment. (Fig. 6.) The roentgenologist considered that the ability of the distal segment to distend and empty constituted strong evidence against Hirschsprung's disease.

The rectal biopsy specimen contained ganglion cells. Laparotomy was performed and the sigmoid

FIG. 6. Case III. Roentgenogram of postevacuation barium enema outlining persistent sigmoidal dilatation despite satisfactory emptying of the colon.

loop was found to be markedly dilated. Hypertrophy was notable especially at the rectosigmoid area. Segmental resection was performed with end-to-end anastomosis. The postoperative course was benign and the patient was discharged on the seventh postoperative day. Ganglion cells were identified in all parts of the resected specimen examined.

Two years after surgery the patient was reexamined. There were no bouts of diarrhea or constipation, bowel habits were normal, and the abdominal tenderness and distention had disappeared.

COMMENTS

Clinical Symptoms. These cases had many features in common, including a history of dietary difficulties, onset of symptoms in early neonatal life, chronic intestinal obstruction [*8,11*], recurrent episodes of diarrhea and normal growth and development.

There were similar findings, including good general health, abdominal distention and empty rectal ampulla. Palpable fecal masses and flaring of the costal margins were present in the two young patients.

In each instance the history and physical findings were consistent in part with the diagnosis of Hirschsprung's disease, and the roentgen features also supported this diagnosis.

Differential Diagnosis. It is necessary to differentiate between segmental fusiform dilatation of the colon and such congenital lesions as duplication, diverticulum and aganglionic megacolon.

Duplications [*3,6,7*] are cystic structures which are contiguous with the bowel and have a common muscular coat and blood supply. The lumen may or may not be connected with the lumen of the functioning bowel. These lesions are related to the period of transition of the embryonic intestine from a solid to a hollow tube structure, which results from the coalescence of vacuoles. There is invariably a septum between the two structures. Symptoms of obstruction are not unusual when a communication is present; a movable, cystic mass is usual when no communication exists. If it is very small in size, it may become the leading point for intussusception.

Diverticula are projections from the intestine and may be congenital [*2,3,9*], such as Meckel's diverticulum [*3,5*], or acquired [*1,10*]. The acquired or pulsion diverticulum is most common in the colon, and is considered to be a degenerative lesion as it occurs only in the aged. Since Meckel's diverticulum is invariably located in the small intestine it cannot be related to these colonic dilatations.

Hirschsprung's disease (congenital aganglionic megacolon) results from malformation of the pelvic parasympathetic system [*12,17*] with absence of ganglion cells in Auerbach's plexuses of the hindgut extending cephalad for variable distances. There is also a curious abundance of nerve fibers which are larger than those seen in normal segments of bowel. Progressive peristaltic waves are absent. In the proximal colon containing normal ganglion cells, there are forceful, progressive peristaltic waves which cause hypertrophy from overwork, and dilatation results here from accumulation of fecal and gaseous contents. Thus, the dilatation occurs in a normal segment of bowel which is proximal to the deficient portion and extends proximally for a considerable distance. It is normal both anatomically and physiologically. Chronic obstruction presents early in life with abdominal distention, fecal impactions and frequently poor nutrition.

Segmental dilatation of the colon, judging from the patient's symptoms, apparently represents a defect in motility of the dilated segment itself with normally functioning proximal and distal segments which are of reasonably normal caliber. This is obvious from the fact that segmental resection is rewarded by a return to normal colonic function. One may postulate many reasons for such a dilated segment based upon neurologic or anatomic variations. There may be a neurogenic factor involved despite the presence of ganglion cells. The symptoms certainly suggest a malfunction which conceivably may be related to an abnormal nerve supply. One must also consider that the function of any particular segment of bowel is related not only to its neurologic components but also to its location, attachments and relationship to other intra-abdominal viscera [*4*]. In Case I, position of the transverse colon was normal but the cecum was on a free mesentery. In Case II, position could be considered normal because the colon was foreshortened and there was no true transverse position of the transverse colon; attachments, however, appeared to be normal. In Case III, the mesentery of the sigmoid was unusually long. In all cases the lesion started and ended abruptly at its proximal and distal bowel attachments.

Pathology. All three specimens were dilated in a fusiform manner, somewhat eccentric in Cases I and II and concentric in Case III. The serosal surfaces were smooth and the taeniae were normal. The specimen measured 8 by 10 cm. in Case I, 13.5 by 22 cm. in Case II, and 40 by 16 cm. in Case III. Grossly, the cut surfaces revealed uniform hypertrophy of the muscle layer. There were no diverticula, points of weakness or defects. The specimen in Case II had an unusual rugal pattern which was concentric in fashion at the point of greatest convexity.

Microscopically, there was a normal laminar arrangement of the muscle coats in all the specimens with mild mucosal and submucosal edema and with unbroken surfaces. The serosa was normal in each case. Numerous sections were made, critically chosen to compare various areas of the resected specimens with controls, and special stains for nerve, muscle and connective tissue were made. No significant changes from normal could be demonstrated either in number or distribution of nerve fibers and ganglion elements. Both were present in abundance throughout the entire length of the specimens and these were cytologically undistinguished. The neuronal elements in both myenteric and submucous plexuses were numerically commensurate with the degree of dilatation of the bowel, and they were well formed.

Recommended Therapy. The preferred therapy is segmental resection. It is particularly valuable to establish the presence of ganglion cells by rapid section before or during the definitive operative procedure because segmental resection is less traumatic than coloproctectomy in such patients, and it is all that is required to effect a cure.

SUMMARY AND CONCLUSIONS

Segmental fusiform dilatation of the colon is a condition not previously described. It should be considered in any patient with an early and substained history of chronic intestinal obstruction, abdominal distention, diarrhea, fecal impactions, Hirschsprung's-like roentgen findings, and adequate growth and development. Rectal biopsy is of great importance especially for surgeons who see only occasional cases of congenital aganglionic megacolon. X-ray interpretation, while frequently classic in Hirschsprung's disease, may be misleading even in experienced hands. Any doubt or confusion about such findings may be easily dispelled by securing a rectal [*13*] biopsy specimen and proving the presence of ganglion cells to rule out Hirschsprung's disease.

Acknowledgment: We wish to thank Dr. Gherardo Gherardi for his kind help in making the pathologic studies and Dr. Carroll Berman for his help in interpreting the radiographic studies.

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Open Chest versus Closed Chest Cardiac Resuscitation

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SLOWLY the domain of cardiac resuscitation is no longer being associated with heart surgery but rightfully has become a useful tool of all surgeons and the medical profession. Cardiac resuscitation as of today is still in its infancy.

Our previous conception of death must necessarily undergo new consideration, because the death factor at times can be small and reversible. The precipitating factor frequently amounts to a minor physiological breakdown, the magnitude of which in certain circumstances is sufficient to produce cessation of the heart beat with consequent fatal deterioration of the cerebral cortex. The basic problem in cardiac resuscitation is to keep the brain viable. In other words, our serious attention must be directed toward the prevention of anoxia in those tissues of the body most sensitive to anoxia. We must never lose sight of this primary consideration.

It is now feasible to perform this procedure in any area, provided a system has been established, proper instruments are available and a trained team is on hand.

In this discussion the steps for the treatment of this cataclysmic disaster will be referred to only briefly, as precise detailed instructions are found in other medical literature [*1*].

In our opinion, the cardinal point in the resuscitation procedure is its separation into two separate and distinct steps. Beck is responsible for this basic contribution. The components are: part I, re-establishment of the oxygen system (the emergency act); part II, restoration of the heart beat. This concept focuses attention upon the oxygen system and not upon the heart beat.

Re-establishing the oxygen system entails three functions: first, getting oxygen into the lungs; second, having enough hemoglobin available to transport the oxygen; and finally, providing a dynamic pump to propel the oxygenated hemoglobin to the brain and other vital organs in order that they remain viable. This emergency act must be established within three to four minutes; otherwise the anesthetized cerebral cortex will be irreversibly damaged.

In the operating room the surgeon is confronted with two conditions of cardiac stoppage, explicitly, cardiac standstill and ventricular fibrillation. The former is more frequent. Ventricular fibrillation has been accepted as the mechanism of death in about 90 per cent of the fatalities from acute coronary occlusion. Recently, Hellerstein and Feil [*2*] reported that ventricular fibrillation occurs in only 20 per cent of sudden deaths from acute coronary occlusion.

In the treatment of cardiac standstill (asystole), efficient massage and good pulmonary ventilation will restore the heart beat and circulation in most instances. Drugs are not the first resort, and they should be used only in the smallest quantities that are effective.

An electronic pacemaker, or heartpacer, can be a valuable machine to have available during the postresuscitative period. Applied to one whose heart is slow and faltering, at times it can control and bolster such a beat. Others have great hopes that this machine, when applied to the exterior of the body, will act as a self-starter for the arrested heart in standstill. Its main value at present has been its use in the Stokes-Adams syndrome or serious heart block.

Our experience in the laboratory, using dogs, leads us to believe that the desired results will not occur when cardiac stoppage has been in effect beyond forty-five to fifty seconds. This

TABLE 1
CARDIAC MASSAGE FOLLOWED BY DEFIBRILLATION

No. of Experiments in Dogs	Breakdown of O_2 System (sec.)	Manual Massage	Defibrillated	Normal Blood Pressure Attained
83	120	Yes	Yes	Yes

type of stimulus applied to a cyanotic and dilated heart has no effect.

Briefly, the treatment of ventricular fibrillation consists of good ventilation, effective massage and the application of a strong electrical current by means of a defibrillating machine. If conditions are right, this will convert the fibrillating or convulsing heart to one with a coordinated rhythm.

A reliable and foolproof shocking device or a defibrillating machine is a necessity. As of now, this is the only practical method which will successfully restore a coordinated beat. Experimentation is being undertaken with the hope that a very strong current applied to the intact thorax will prove to be an effectual approach in the treatment of this desperate condition.

The use of defibrillating, shocking and pacemaker machines necessitates that we, as doctors, have some conception of safe current values. As has been widely known and demonstrated, electrical currents can be not only beneficial to the heart but also extremely hazardous and harmful. As paradoxical as it may seem, so-called weak currents like house current, fall into this latter classification. In the human, current values of 50 to 150 ma., upon reaching the heart, usually produce ventricular fibrillation which terminates in instant death.

Currents above 200 ma. can cause burns, muscular contractions and paralysis of the respiratory center, but they prevent ventricular fibrillation. At the moment the current is broken, the heart is defibrillated. The application and then the break of this current functions similar to a defibrillating machine. This accounts for the incredible recoveries occasionally reported from short contacts with excessively strong currents. How much current flows through the body depends upon the nature of the contact. Ordinarily, 10 to 20 per cent of the total current flows directly through the heart. It would appear that criminals undergoing judicial electrocution forfeit their lives from the thermal effects of the electricity, particularly upon the brain.

We have undertaken experiments concerned with restoring a coordinated cardiac rhythm in dogs' hearts which have been placed in a state of ventricular fibrillation. An attempt to evaluate two methods for defibrillation and the restitution of the circulation has been made.

In one series of eighty-three lightly anesthetized dogs (Table 1) ventricular fibrillation was produced by the direct application upon the heart's surface of a weak, 110 volt, alternating current (about 25 ma.). In each instance manual massage and pulmonary ventilation was instituted exactly two minutes after the development of the fibrillation. In every instance the normal heart rhythm was readily restored to this well oxygenated heart by an electrical countershock of 110 volts and approximately 2.5 amp. All eighty-three dogs survived and were normal in all respects within less than twenty-four hours.

External defibrillation of the heart within the intact chest was carried out in another series of experiments on forty-one dogs. The stoppage of the heart was put into effect by an electrical current of 110 to 220 volts applied to the shaved chest of the animal.

This cessation of the cardiorespiratory system was carried out under what were considered to be ideal circumstances for resuscitative procedures. Arrest was sudden, anesthesia had been light, special instruments and oxygen equipment were at hand, and no previous tests had been made upon the animal.

The onset of ventricular fibrillation was determined by electrocardiographic records and by an abrupt fall of blood pressure to zero as recorded by the electrical intra-aortic manometer.

The method of defibrillation consisted of the application of an electrical shock to the closed or intact and shaved chest of a dog. Special large heavy electrodes delivered 980 to 1,000 volts (10 to 12 amp.) through the chest for 0.1 seconds.

In those tests in which there had been a breakdown of the oxygen system for only thirty seconds, following a countershock, invariably there was a prompt satisfactory return of blood pressure to normal and the electrocardiogram indicated a supraventricular rhythm.

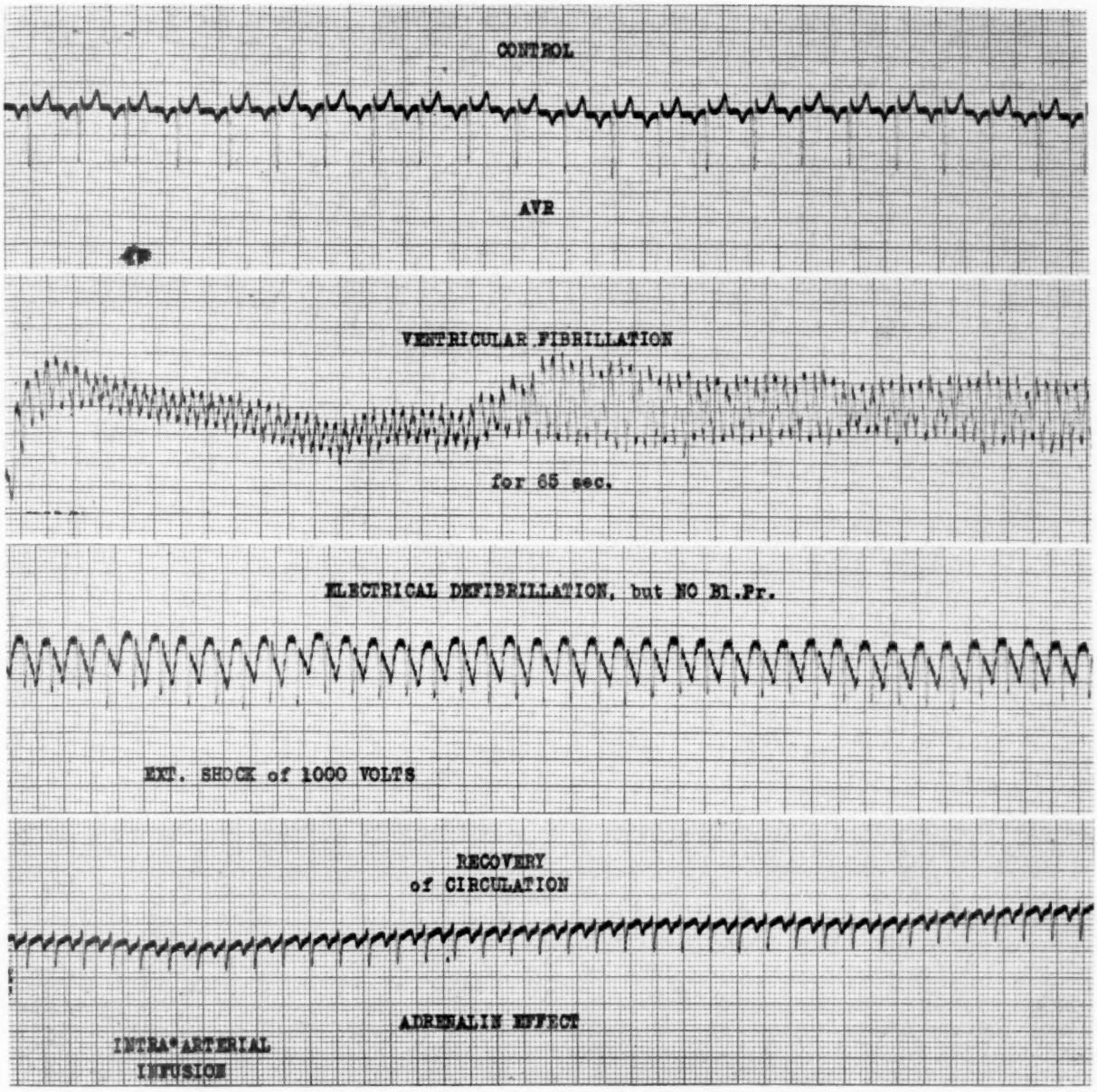

FIG. 1. Electrocardiogram of successful external defibrillation.

As indicated in Table II, somewhere around fifty seconds is the dividing line between satisfactory and unsatisfactory defibrillation by the external application of a countershock in these experiments. This is in general agreement with Dow and Wiggers' [3] report in 1940. Beyond this point, it was found that the heart could always be defibrillated, as indicated by the electrocardiogram (Fig. 1), but there was seldom return of a satisfactory blood pressure or pulse. In this situation it was found that rapid surgical exposure of the heart, followed by a short manual pumping of the heart, readily and successfully restored the heart beat, blood pressure and the circulation to a normal level. In other experiments (Fig. 1), after electrical defibrillation had been recorded and no return of systemic circulation occurred within ninety seconds, the administration of an intra-arterial infusion of saline and 1:10,000 dilution of Adrenalin® under pressure of 300 mm. Hg resulted in a satisfactory return of systemic circulation without opening the chest.

It is known (but too often overlooked) that electrical activity, as recorded in the electrocardiogram, is not necessarily related to the

TABLE II
DEFIBRILLATION BY EXTERNAL ELECTRODES

No. of Dogs in Experiment	Duration (sec.)	E. K. G. Defibrillation	Return of Pulse and Blood Pressure (No.)	Open Chest Massage (No.)	Normal Blood Pressure Attained (No.)
1	15	Yes	1	0	.....
1	25	Yes	1	0	.....
4	30	Yes	4	2 assisted	4
4	35	Yes	3	2	5
8	45	Yes	3	5	8
5	55	Yes	2	2	4
5	60	Yes	2	5	5
6	65	Yes	0	4 (Fig. 1)	4 (Fig. 1)
4	75	Yes	1	3	4
3	90	Yes	0	3	3

effectiveness of the circulation or survival. It also appears that it is a minor problem actually to defibrillate the heart by this means. However, to restore the life functions of the animal after fifty-five seconds, supplemental measures had to be taken, such as cardiac massage or arterial transfusion or infusion directed toward the base of the heart. These supplemental measures will transport oxygen into the coronary system and into the myocardium. The myocardium will remain viable for well over an hour, but in order that it may function it must have oxygenated blood in its capillaries. The addition of an outside source of electrical stimuli (pacemaker) to enhance the effectiveness of the heart beat under the condition of a cyanotic myocardium is not the simple or final answer.

In another series of experiments, seventy separate dogs were used. (Table III.) The heart was thoroughly exposed. Fibrillation was produced by the application of a weak current directly to the ventricles of the heart. These seventy hearts were allowed to remain in ventricular fibrillation for exactly 120 seconds. Thereupon, electrodes were directly and firmly applied to the ventricles and a countershock of 110 volts and approximately 2.5 amp. were delivered. Electrical defibrillation* was readily produced in each instance, but the heart remained motionless and there was no circulation of blood. After a short period of manual massage the blood pressure and circulation returned to normal levels.

* Pulmonary ventilation of 100 per cent oxygen had been instituted at the moment of defibrillation.

TABLE III
DEFIBRILLATION BY DIRECT APPLICATION OF ELECTRODES TO MYOCARDIUM

No. of Dogs in Experiments	Duration (sec.)	E. K. G. Defibrillation	Return of Pulse and Blood Pressure (No.)	Open Chest Massage (No.)	Normal Blood Pressure Attained (No.)
70	120	Yes	0	70	70

REPRESENTATIVE PROTOCOLS

Dog No. 58-5. On January 7, 1958, a 26 pound male dog was placed under light ether anesthesia with the aid of an intratracheal tube and a Rand-Wolfe respirator. The neck and both sides of the chest were clipped and shaved. The jugular vein was isolated for intravenous therapy and the carotid artery for manometric readings of blood pressure. The dog was given 5 cc. of heparin intravenously to prevent clotting in the cannula of the manometer. Electrocardiograms were taken except during the periods when shock was applied. Fibrillation was produced by applying 160 volts of alternating current externally through the intact chest wall and noting the fall in blood pressure along with the characteristic electrocardiographic pattern. Blood pressure was 104 mm. Hg.

Fibrillation was produced and was allowed to continue for forty-five seconds. External countershock of 1,000 volts was applied with immediate defibrillation and a return of blood pressure to a higher than normal level.

After ten minutes ventricular fibrillation was again produced and allowed to continue for sixty-five seconds. Countershock was applied. An electrocardiogram revealed electrical defibrillation; but no recordable pulse or blood pressure. After three and a half minutes the chest was opened and massage was begun: 1.5 cc. of 1:10,000 Adrenalin was injected into the chamber of the heart after four and three-quarter minutes. A coordinated beat was noted. The blood pressure rose rapidly to 160 mm. Hg at five and a half minutes and then leveled off at 110 mm. Hg at seven and a half minutes. After nine minutes it remained stable at 96 mm. Hg.

Dog No. 57-182. On November 27, 1957, a 22 pound female dog was placed under light ether anesthesia, administered intratracheally with the

aid of a Rand-Wolfe respirator. Intravenous saline drip was begun with Levophed® 1:300. Ventricular fibrillation was produced by external shock of 160 volts of alternating current, and was allowed to continue for forty-five seconds. A countershock of 1,000 volts was applied to the closed chest. The electrocardiogram revealed a return to normal rhythm, but there was no recordable pulse or blood pressure. The chest was opened after cessation of circulation for one and a half minutes. The heart was found in asystole. Manual massage was started after two and a half minutes, and 1 cc. of 1:1,000 Adrenalin was injected into the chamber of the heart. Good beat was obtained in five minutes. Blood pressure was 120 mm. Hg in eight minutes.

SUMMARY

1. External defibrillation was attempted in experiments on forty-one dogs. In all instances the heart could be readily defibrillated, as indicated by the electrocardiogram. However, a return of pulse and blood pressure seldom occurred beyond a fifty-second time limit.

2. In experiments on seventy dogs the heart was permitted to fibrillate for 120 seconds before a countershock was directly applied. Electrical defibrillation promptly occurred but there was no return of systemic blood pressure. Following immediate massage there was a quick return of a coordinated beat and a normal blood pressure.

3. In experiments on eighty-three dogs the heart was allowed to fibrillate for 120 seconds; then ventilation and massage were instituted before a direct countershock was applied to the ventricles. This was followed in each case by normal circulation and eighty-three survivals.

4. For successful cardiac resuscitation, the re-establishment of the oxygen system is the primary act and the restoration of the heart beat is secondary.

5. It appears that it is a minor problem to defibrillate the heart through an intact chest. However, to restore the life functions of an animal after some fifty seconds, supplemental measures have to be taken such as cardiac massage, or intra-arterial transfusion or infusion.

6. Under ideal circumstances, when a trained team and equipment are in readiness in a room, a few seconds spent on external countershocking might be conceivable. We are carrying out additional studies continuously.

Acknowledgment: We are indebted to Dr. David Leighninger for technical assistance.

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Studies on the Phrenic Nerves and the Diaphragm of the Dog

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THE phrenic nerves have been of particular interest to physiologists for their role in respiration, and to surgeons for their use in the treatment of pulmonary tuberculosis, diaphragmatic hernia, cardiospasm, and other upper gastrointestinal disturbances [1–3].

Investigations of the phrenic nerves in relation to gastrointestinal functions have been a major project of our group, in the course of which we have encountered the problem of trophic effects of a nerve on striated muscle.

THE PHRENIC NERVES AND RESPIRATION

The origin of the phrenic nerve seems to vary with each species of mammals. In the dog, it derives from three roots of the ventral division of the fifth, sixth, and seventh cervical nerves. The branch from the seventh cervical nerve joins the main phrenic trunk usually on the medial surface of the first rib; very rarely an accessory phrenic nerve presents itself completely separate from the main nerve throughout the entire course, innervating the lumbar part of the diaphragm [4]. The trunk of the phrenic nerve enters the thoracic cavity ventral to the subclavian artery and passes through the pericardial mediastinum, crossing the pericardium ventral to the root of the lung. The left nerve runs its entire course in the pericardial mediastinum to the diaphragm, whereas the right nerve runs along the lateral aspect of the vena cava and is therefore not contained within the mediastinal septum but in the special fold of the pleura provided for the vein. Shortly before reaching the diaphragm (approximately 2 to 3 cm. above), each phrenic nerve divides into three main branches, the ventral, lateral and dorsal divisions; each upon reaching the diaphragm penetrates into it and, running under its serosal surface, subdivides into finer branches.

At its origin, the phrenic nerve in the dog (and in man) is a pure cerebrospinal nerve, consisting of motor and sensory fibers. It receives sympathetic fibers from the inferior cervical ganglion and sometimes also from the medial cervical and the first thoracic ganglion. In the diaphragm, phrenic nerve fibers unite with sympathetic fibers from the celiac ganglion. On the right side a phrenic ganglion below the diaphragm has been described in man, containing sympathetic and phrenic fibers; I have not been able to find the ganglion in the dog.

The ventral, lateral and dorsal divisions of the phrenicn erve innervate, respectively, the anterior (the sternal part and the anterior portion of the costal part), the lateral (the lateral portion of the costal part), and the posterior parts (the lumbar or crural part) of the diaphragm. Occasionally, however, the lateral lumbar part of the diaphragm is innervated by a branch of the lateral division of the phrenic nerve. Each one of the phrenic nerves innervates its own side of the diaphragm, with one exception to be mentioned herein.

The present terminology concerning the crura of the diaphragm assumes that they originate from the spine and are inserted into the central tendon. However, I agree with Collis et al. [5], that the anatomy of the crura is better understood if they are thought to arise from the central tendon and the esophagus is considered as a midline structure; accordingly, I believe that in the dog the muscle bundles arising from the left half of the central tendon are innervated by the left phrenic

nerve, and therefore, should be called the left crus, although part of these muscle bundles attach to the right side of the lumbar spines.

In 25 to 30 per cent of dogs, a portion of the right crural part of the diaphragm, a muscle bundle on the immediate right side of the esophageal hiatus, receives a small "crossing branch" of the posterior division of the left phrenic nerve [6,7]. It would be of interest to know whether a similar cross innervation exists in man. In the dog, the right phrenic nerve has never been observed to send a crossing branch to the left side of the diaphragm. There seems to be no cross innervation to the sternal part of the diaphragm, although it has been reported in another mammal by Strauss [8].

The diaphragm of the dog is not only innervated by the phrenic and the cervical sympathetic fibers contained in it, as well as by abdominal sympathetic nerves, but it also receives branches from the lower five or six intercostal nerves (the ninth to thirteenth, occasionally also the eighth). Claims [3,9] that the diaphragmatic branches of the intercostal nerves contain motor as well as sensory fibers have been disproved by others ([8,10,11] and by ourselves; in the dog, the intercostal nerves send only sensory fibers to the peripheral portion of the diaphragm. Therefore, it can be said that the phrenic nerves are the only nerves that supply the diaphragm with motor fibers.

There have been reports ([12] and others) describing the reappearance of regular respiratory contraction of the diaphragm in man from one and a half to two years after phrenic exeresis in the neck. This mechanism was postulated to be through the twelfth intercostal nerve and through sympathetic innervation. Now that the phrenic nerve has been found to be the only motor nerve of the diaphragm, this postulation is undoubtedly wrong. Failure to secure paralysis of the diaphragm is regarded as the failure to include the accessory phrenic nerve when the nerve is avulsed in the neck. In the dog, reappearance of respiratory contraction of the diaphragm after phrenic exeresis in the chest has never been observed. Following crush of the phrenic nerve in the dog, however, it regenerates and the diaphragm reactivates in three to six months. After phrenicotomy, when the nerve is simply cut, we have observed several times that the cut ends have reconnected spontaneously and resumed normal function, even if the cut ends had been displaced considerably from each other at the time of the operation. Chemotaxis may play a role in this phenomenon.

Section of a phrenic nerve leads to paralysis of the ipsilateral hemidiaphragm, which soon stops contracting upon stimulation of the distal stump of the cut phrenic nerve; its dome rises considerably and may continue to rise for six months [13]. Paralysis of the entire diaphragm by bilateral phrenicotomy does not seriously interfere with respiration of the dog, which is quite normal even with moderate activity. Opposing results appear to be due to faulty techniques [14]. It seems, therefore, that in the dog at least diaphragmatic contraction cannot be regarded as of supreme importance in respiration. This principle has been applied to man, i.e., bilateral phrenic crush has been performed for treatment of persistant singultus without appreciable postoperative respiratory difficulty, when physical exercise was restricted; excessive swallowing or aspiration of air was counteracted by the use of a Levin tube or enemas [15].

TROPHIC AND FUNCTIONAL EFFECTS ON THE DIAPHRAGM

The diaphragm is innervated by the phrenic nerves with their cervical sympathetic fibers, by branches of the lower intercostal nerves and by fibers from the abdominal sympathetic nerves. Therefore, it has been assumed that each of these nerves, especially the sympathetic nerves, participates in trophic maintenance of the musculature of the diaphragm [11,16–18]. However, our own work does not support this assumption [7,19–22], but is in accord with the work of others [8,10,23].

Unilateral phrenic exeresis is followed by atrophy of the ipsilateral hemidiaphragm in periods of three to four months. In the majority of cases, the entire hemidiaphragm is involved in this process. However, a few exceptions are probably responsible for the controversy on exclusive trophic effect on the diaphragm by the phrenic nerves; an occasional lack of atrophy at the crural part after section of one phrenic nerve or the spinal roots of one phrenic nerve was attributed to trophic effects of branches of the abdominal and cervical sympathetic nerves respectively and of the intercostal nerves.

In our experiments on dogs, the only cases in which a portion of the hemidiaphragm failed to

atrophy after exeresis of one phrenic nerve were either due to cross innervation by the left phrenic nerve to the right crural part of the diaphragm or due to an accessory phrenic nerve which had been left intact. Furthermore, interruption of the phrenic nerve in the cervical region is unreliable because not all branches of the nerve may be found. These factors may be responsible for the aforementioned "exceptional observations" which caused controversy. Following section of the lower six intercostal nerves, as well as four months after celiac ganglionectomy, no evidence of degeneration of any portion of the diaphragm was observed in my experiments on dogs.

It can be concluded, therefore, that the phrenic nerves are solely responsible for the trophic maintenance of the musculature of the diaphragm. This is in accord with the statement by Tower [*24*] that degeneration of striated muscle follows only motor denervation.

After exeresis of one phrenic nerve, the ipsilateral diaphragmatic muscle begins to atrophy, with complete degeneration after ten to twelve months. If the cut ends of the phrenic are anastomosed primarily, the muscle of the diaphragm shows only a mild degree of degeneration and later regenerates to normal. When a phrenic nerve is cut approximately 5 cm. above the diaphragm and anastomosed primarily, it takes seven to eight weeks for it to regenerate and for the appearance of contraction of the diaphragm upon electric stimulation of the nerve, although it takes eleven to thirteen weeks before spontaneous respiratory function of the diaphragm recurs. The same trend is seen in the case of phrenic crush. Therefore, it may be assumed that, even before the anastomosis becomes functional, some degree of a trophic effect is present, protecting the musculature of the diaphragm from severe and irreversible degeneration before a functional anastomosis is established. This may be due to a humoral substance which travels down in the nerve sheath [*25–27*]; our most recent work [*28*] indicates that more probably the phenomenon is connected with reinnervation of the diaphragm by new nerve axons, representing possibly a primary stage of regeneration adequate for trophic maintenance but not for the transmission of impulses from the respiratory center to the diaphragm.

If the vagus nerve is cut below the recurrent laryngeal nerve and its proximal stump anastomosed to the distal stump of the phrenic nerve, contraction of the diaphragm upon stimulation of the vagus nerve above the anastomosis or of the distal phrenic nerve occurs four to five months after the operation, although at that time the diaphragmatic musculature was found to be thin and yellowish and showed no spontaneous respiratory motion. Histological study showed no more than mild atrophy of the muscle tissue and suggests that this atrophy is of the disuse type. Others have reported that respiratory motion of the diaphragm is resumed as early as fifteen days after the same type of vagophrenic anastomosis [*14*]. We have never seen return of respiration with this procedure in dogs observed for periods of more than one year [*28,29*]. We cannot completely explain this discrepancy in results, but we know that fluoroscopic observations of diaphragmatic motion in dogs are very unreliable and can be misleading.

Anastomoses between an intercostal nerve and a phrenic nerve have been performed on ten animals. It seems to take somewhat longer for this kind of anastomosis to become functional than phrenophrenic anastomosis. In a dog examined twelve weeks after intercostal-phrenic anastomosis, the diaphragm contracted upon stimulation of the anastomosed nerve. Fluoroscopically, spontaneous motion of the diaphragm was observed twenty-one weeks after the anastomosis. The presence of spontaneous motion of the diaphragm was confirmed by exploratory thoracotomy and direct observation; the diaphragm showed active, rhythmic contractions when artificial respiration was stopped temporarily. The latter procedure is necessary because in normal dogs, under artificial respiration with the chest opened, the diaphragms do not show respiratory motion unless artificial respiration is interrupted for a short time.

Guth and Frank [*30*] observed restoration of diaphragmatic function after anastomosis between the proximal vagal stump above the branching of the recurrent laryngeal nerve and the distal phrenic stump in the rat. This is in accord with our experiments because the vagus nerve at that level contains motor fibers which transmit impulses from the respiratory centers. We are presently studying anastomosis between the long thoracic nerve and the phrenic nerve, which we expect to lead to restoration of diaphragmatic contraction for the same

reasons as in the case of the recurrent laryngeal and intercostal nerves. Colledge and Ballance [31] anastomosed the hypoglossal nerve to the distal phrenic stump and observed diaphragmatic contractions using only fluoroscopy which is, as previously mentioned, unreliable.

Duncan and Eanes [32] observed in the cat and rat that the accessory, the long thoracic and the facial nerves, anastomosed to the distal phrenic nerve, supplied motor fibers to the diaphragm, but they did not observe rhythmic contractions of the diaphragm.

Phrenovagal anastomoses were performed in dogs and fourteen to twenty months later the animals underwent fluoroscopy and reoperation, in order to check nerve function [33]. One dog died spontaneously with tremendous dilation of the stomach and a number of ulcers around the cardia. The other animals had no respiratory movements of the left side of the diaphragm, and the stomach showed no evident effects of a functioning phrenovagal anastomosis. However, upon prolonged stimulation of the phrenic nerve above the anastomosis, the stomach showed distinct contractions. Sections of the nerve demonstrated fibers grown from the phrenic nerve into the vagus stump.

EFFECTS OF PHRENIC NERVES AND DIAPHRAGM ON GASTROINTESTINAL FUNCTIONS

Untoward symptoms following phrenicotomy or phrenic exeresis performed for treatment of pulmonary tuberculosis, described by Sauerbruch [2] and later named Roemheld's syndrome [34], consist of bradycardia, premature systoles, anxiety, epigastric distress, anorexia, pallor, nausea, vomiting and eructations. This syndrome has never been observed in our experiments on dogs. Noack [12] believes that the syndrome is due to the incidental tearing of sympathetic nerve fibers during phrenic avulsion in the neck and not to interruption of the phrenic nerve itself.

Following left phrenicotomy (or phrenic crush) in the dog, shortening of gastric emptying time by 20 to 60 per cent (average 30 per cent) was observed. Fluoroscopically, the gastric dome follows the elevated diaphragm resulting in a more vertical position of the stomach and a large air bubble in the fundus, conditions which may explain faster gastric emptying. The latter returns to normal in periods varying from several weeks to months depending on whether the nerve is crushed or cut [4,29].

Left phrenicotomy or phrenic crush in the dog abolishes gastric distention and the retention usually observed following bilateral vagotomy. This has been applied successfully to man [15,35]. High section of both vagi in the dog (below the hilum of the lungs) is followed by cardiospasm, which was prevented or alleviated by simultaneous section of the left phrenic nerve [36]. Therefore, left phrenic crush has been used in clinical cases of cardiospasm especially when fibrosis of the esophagus has not yet occurred. In cases of painful diaphragmatic hernia with bleeding ulcer and in persistent cases of singultus, left or bilateral phrenic crush has been used successfully [15].

Right phrenic section or exeresis produces elevation of the pylorus and duodenal bulb as high as the gastric cardia and a marked elevation of the liver and gallbladder, but gastric emptying or function of the gallbladder are not affected [37,38].

SUMMARY

The anatomy and physiology of the phrenic nerves and the innervation of the diaphragm are reviewed in the light of recent work.

The effects of section of the phrenic nerve on function of the diaphragm and recovery of the diaphragm following anastomosis of a cut phrenic nerve are described.

The trophic maintenance of the diaphragmatic musculature by the phrenic nerve is described. The role of sympathetic and intercostal nerves in this phenomenon is reviewed critically and the conclusion is reached that normally the phrenic nerves are the only nerves having trophic effects on the diaphragm. However, anastomosis of the distal phrenic nerve with the central end of another nerve (intercostal, recurrent laryngeal, vagus) is able to maintain a trophic effect.

A number of effects of interruption of phrenic nerves on gastrointestinal function and the clinical applications of our results are reported.

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Microscopic Variables in a "Standardized" Laparotomy Wound in the Rat

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We have previously tried to gauge the tensile strength of midline laparotomy wounds in rats by an abdominal bursting technique and two traction methods. In each instance there was greater variation in the values obtained for comparable wounds than we had anticipated. The present study was undertaken, in part, to determine whether microscopic variables existed which might explain our experience with tensile strength determinations.

MATERIALS AND METHODS

Forty growing Wistar male rats of similar size, weighing approximately 200 gm., were used in these experiments. They were fed a standard commercial rat chow with water *ad lib.* Ten animals of the forty were sacrificed without experimental wounding to study the anterior midline abdominal area. All others were wounded and sutured in as identical a fashion as possible by the same operator. Midline laparotomy wounds 4 cm. in length were made aseptically under light ether anesthesia. The wounds were sutured with through and through sutures of fine stainless steel. No postoperative dressings were applied. The animals were sacrificed (by overdosage of ether) in groups of ten at seven, ten and fourteen days postoperatively, and the wound areas were excised, pinned to a board and fixed in 10 per cent neutral formalin. Tissue sections were taken transversely from the mid-level of the wound and prepared with usual histological methods. Harris' hematoxylin and alcoholic eosin, Wilder silver, and Rinehart modification of the Hale colloidal iron staining techniques were used routinely. Verhoeff's elastic tissue stain was used in a lesser number. During the microscopic examination the midline area epidermis to parietal peritoneum in one dimension and the area between the rectus abdominis muscles in the other was measured with the aid of an ocular micrometer.

RESULTS

Normal Midline, Anterior Abdominal Wall. The skin contained a number of hair follicles and sebaceous glands. An estimation of the phase of the skin cycle [5] revealed six specimens to be in the anagen phase, one in the catagen phase and two in the telogen phase. One was considered in the transition between anagen and catagen. The appendages were distributed throughout fairly coarse dermal collagen arranged in interlacing bundles. The subcutaneous tissue was mixed fatty and areolar in character. It was sometimes divided in a transverse plane by a layer of superficial muscle, the cutaneous maximus portion of the panniculus carnosus. Thus the collagen sheath of the cutaneous maximus was separated from that of the subjacent rectus abdominis muscle by a layer of fatty and areolar tissue. The cutaneous maximus muscle crossed the midline as an uninterrupted layer in two animals. (Fig. 1.) The external oblique blended with the rectus abdominis muscle lateral to the midline and was also distinctly separated from the previously described superficial muscle layer. The aponeu-

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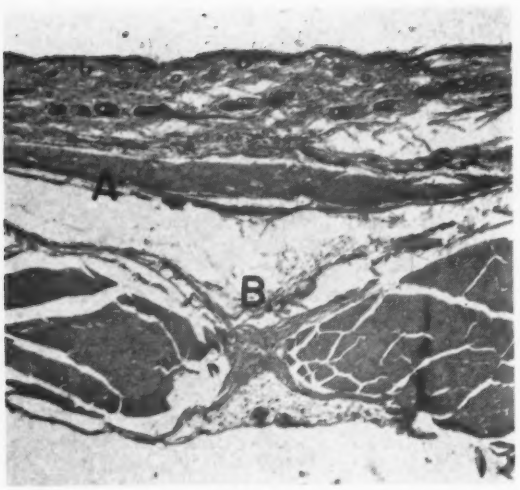


FIG. 1. Normal control, not operated upon. Midline abdominal area; cutaneous maximus muscle (*A*) crosses the midline; linea alba at (B). Hematoxylin-eosin stain. Original magnification, × 35.

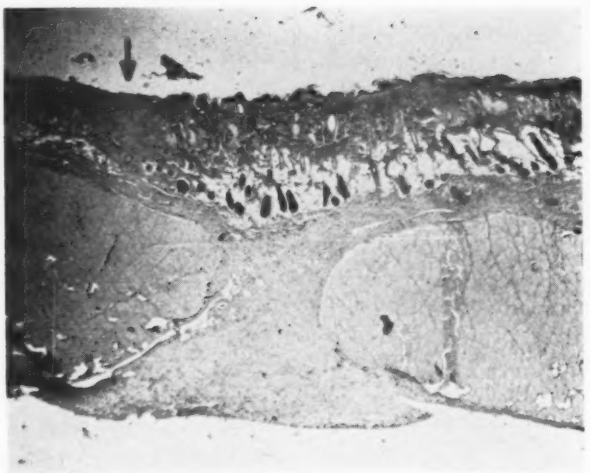


FIG. 2. Step-shaped or shelf-like wound, age of wound, seven days; arrow indicates incision in epidermis and derma. Hematoxylin-eosin stain. Original magnification, × 35.

rosis of the internal oblique and transverse abdominis muscles was distributed beneath the rectus abdominis and could not be identified as a layer separate from the lower surface of the rectus abdominis sheath. The collagen in the subcutaneous fatty and areolar tissue was fine and fibrillar in character. In the muscle sheaths the collagen was coarse, laminated rather than interlacing as in the derma, and compact. The linea alba was composed of similar appearing collagen usually fusing imperceptibly with that of the muscle sheaths. The subcutaneous fatty and areolar tissue separated it from the derma. The collagen in the linea alba was mixed with fat and loose areolar tissue to a variable degree by contrast with that of the derma which was compact and more uniform in amount. The deepest layer of the anterior abdominal wall was composed of the parietal peritoneum. This was infiltrated in all ten animals by a wedge-shaped collection of fat separating the parietal peritoneum from the base of the linea alba. In one animal this collection of fat contained a small lymph nodule. Most midline areas were buttressed on each side by fairly closely approximated rectus abdominis muscles. However, in one animal the muscles were separated to a greater degree than in the others. Measured in ocular micrometer units,* this animal showed a separation of 3½ units compared with a maximum of 1½ in the other nine animals.

In summary, a midline laparotomy wound

* Three units approximately equal to 1.0 mm.

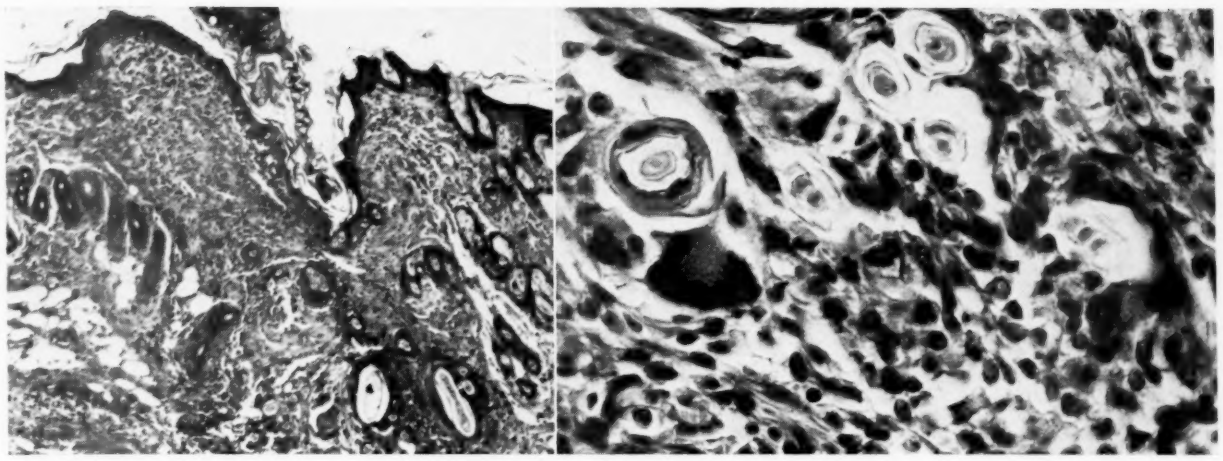
TABLE 1

MICROSCOPIC VARIABLES

Groups	Total No. Animals	Cutaneous Maximus Muscle Crossing Midline	Lymph Nodules in Midline	Widely Separated Rectus Abdominis Muscle	Shelf-Shaped Wounds	Deep Infection*	Involvement of Skin Appendages	Involvement of Rectus Abdominis Muscle	Epidermal Pocket over Wounds
Unoperated controls....	10	2	1	1	..	..	..	..	..
Seven-day wounds.....	10	1	0	3	3	2	5	3	1
Ten-day wounds.....	10	2	3	3	4†	4	1	4	2
Fourteen-day wounds..	10	0	1	2	2	3	2	3	3

* Not apparent on gross inspection.

† One wound of this group was bifurcated.



3 4

FIG. 3. Wound extends diagonally from base of epidermal pocket and encroaches on several hair follicles. Hematoxylin-eosin stain. Original magnification, × 80.

FIG. 4. Deeper in same wound as shown in Figure 3; demonstrates foreign body giant cells and increased cellular reaction. Hematoxylin-eosin stain. Original magnification, × 530.

would incise epidermis, dermis with its appendages, subcutaneous fat and loose areolar tissue, a superficial layer of muscle, the cutaneous maximus (occasionally), linea alba, parietal peritoneum, and occasionally midline lymph nodules located in the parietal peritoneal fat. In four of ten animals a microscopic variable with possible effect on the tensile strength of such a wound was found. (Table 1.)

Midline Laparotomy Wounds. Microscopic examination of the wounds sectioned through the mid-level revealed the majority to be vertical or slightly oblique in configuration. However, in nine animals the wound was step-shaped or shelf-like in outline. (Fig. 2.) The midline derma had been moved inadvertently lateral to its normal position at the time of incision, and thus the dermal wound was made to the right or left of the midline. Orientation was restored in the deeper part of the wound as the linea alba and peritoneum were sectioned. Therefore such a wound was increased in extent over the others by this lateral displacement of the dermal portion.

In most wounds the dermal portion was difficult to trace except where it involved hair follicles. The Rinehart staining technique outlined it best. The cellular reaction to wounding showed a tendency to spread laterally through the subcutaneous fat. The regularity of the wound outline in the linea alba was also affected by the amount of fat and loose areolar tissue in that area. A lateral spreading cellular reaction was usually found in the fat wedge between the base of the linea alba and the parietal peritoneum.

The cellular population that developed as a reaction to wounding consisted mainly of fibroblasts, undifferentiated perivascular cells and endothelial cells. Together these cells comprised approximately 80 per cent of the total in differential counts. Less commonly, histiocytes, lymphocytes, neutrophilic polymorphonuclear leukocytes and mast cells were noted. The concentration of neutrophilic polymorphonuclear leukocytes was increased in nine wounds. We should like to stress here that no wounds of either seven, ten or fourteen days' duration exhibited gross evidence of infection. In wounds involving hair follicles, eosinophils and foreign body type multinucleated giant cells were observed (Figs. 3 and 4). Wound repair as manifested by fibril deposition and maturation to collagen fibers was best studied with the Wilder and Rinehart staining methods. Impairment was noted in areas of deep infection and/or injured skin appendages. Such zones showed positive Prussian blue reaction with the Rinehart method and a lack of fibril deposition or fiber maturation. Although fibril deposition was not impaired in incised muscle, the distribution of fibrils was irregular. Near the peritoneal end of the wound a positive Prussian blue reaction was almost invariably encountered in seven-day wounds. The other levels of the wound were negative in this respect.

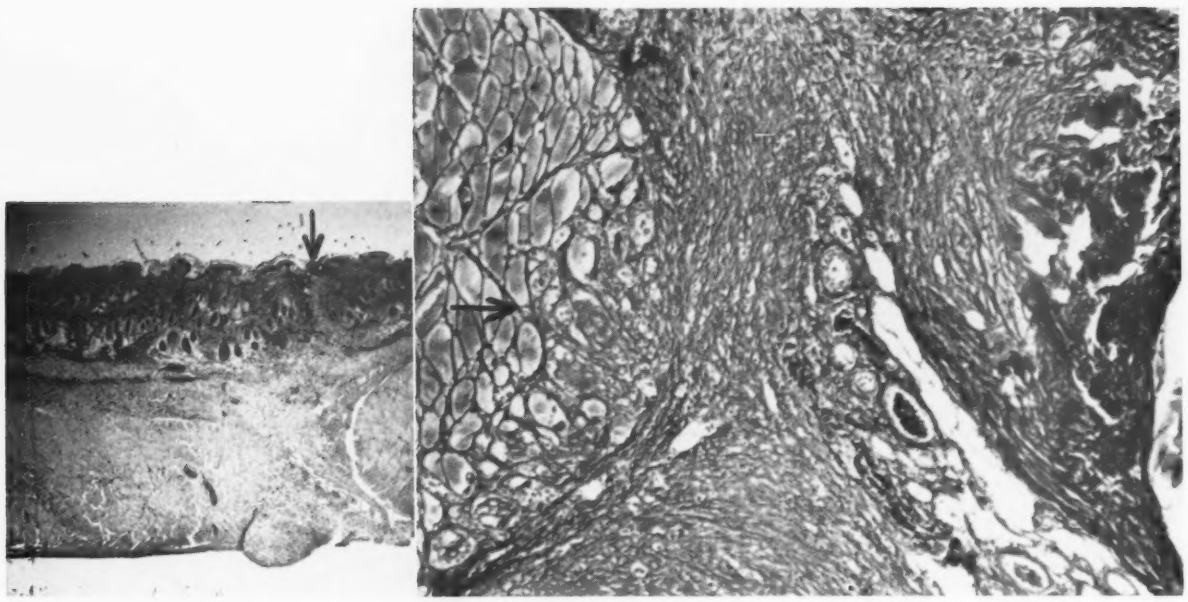


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FIG. 5. Seven-day well buttressed wound involving rectus abdominis muscle on one side. Hematoxylin-eosin stain. Original magnification, × 25.

FIG. 6. Silver-stained section, same wound as in Figure 5 but with higher magnification. Arrow indicates involvement of rectus abdominis muscle on one side. Original magnification, × 80.

FIG. 7. Fourteen-day wound with epidermal pocket; wound also penetrates rectus abdominis muscle on one side. Hematoxylin-eosin stain. Original magnification, × 45.

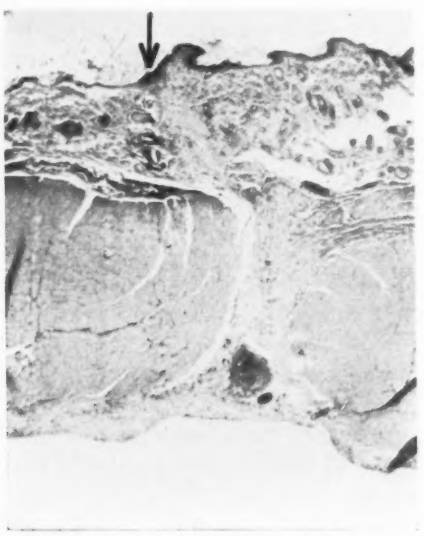

FIG. 8. Ten-day shelf-like wound involves a parietal peritoneal lymph node. Hematoxylin-eosin stain. Original magnification, × 25.

In the series of thirty wounds, twenty-one were believed to be in the anagen phase of the cycle and three in the catagen phase. In the remaining six a decision could not be reached; five appeared to be in transition between anagen and catagen, the other between catagen and telogen. Three wounds involved the cutaneous maximus muscle which crossed the midline in these animals only. Hair follicle and/or sebaceous gland involvement in the incision was present in eight wounds. In five of these wounds

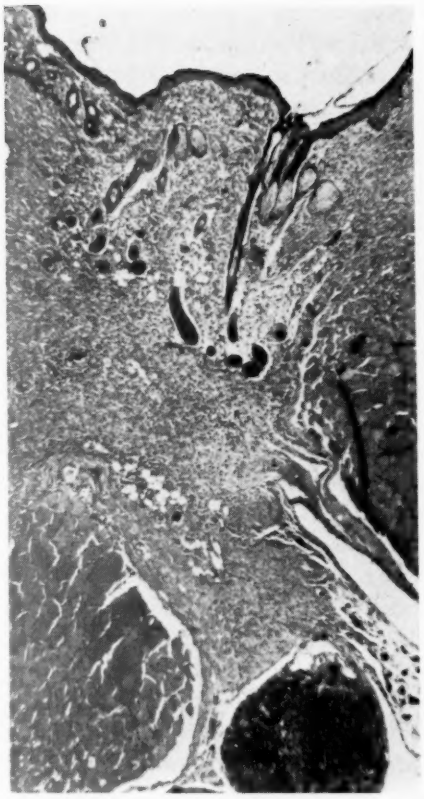

FIG. 9. Ten-day wound with moderate complicating infection and lymph nodules near the parietal peritoneum. Hematoxylin-eosin stain. Original magnification, × 45.

the skin was in the anagen phase of the cycle, one in transition between anagen and catagen, and in the other two in catagen. The wound penetrated the sheath of the rectus abdominis muscle and involved the muscle fibers in ten wounds. (Figs. 5 and 6.) In nine wounds deep infection* was manifested by increased cellularity. One was complicated by surface ulceration. In two wounds an epidermal pocket with exudate was found. Five of the wounds with deep infection were in anagen, three in transition between anagen and catagen and the other in transition between catagen and telogen. Both wounds with epidermal pockets containing exudate were in the anagen phase. There were four others with epidermal pockets containing keratinized material only. (Fig. 7.) Lymph nodules were present in the midline parietal peritoneum and were involved in or abutted on the line of incision in four wounds. (Figs. 8 and 9.) In the majority of wounds the margins were

* Infection of sutures was not tabulated unless the suture infection had spread to involve the laparotomy wound.

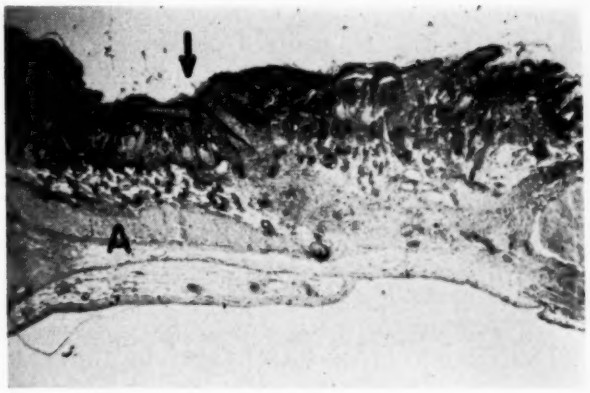

FIG. 10. Diagonal, poorly buttressed seven-day wound in thin, fatty midline with widely separated rectus abdominis muscles; cutaneous maximus muscle on left (A). Hematoxylin-eosin stain. Original magnification, × 25. (Compare with Figure 5.)

fairly closely approximated and buttressed by apposing rectus abdominis muscles, but in eight animals the rectus abdominis muscles were rather widely separated and the midline was thin and appeared poorly supported in this respect. (Fig. 10.) In these rats the rectus abdominis muscles were separated for 3½ units in three wounds, 4 units in two, 5 units in two and 13 units in the other. Only four wounds were free from one of the complicating variables described. Ten wounds had one variable, eight had two, three had three, four had four, and one had six.

COMMENTS

Tensile strength determinations as an index of wound healing have interested surgeons for many years. The fact that new methods are being developed and reported is perhaps an indication of the need for a better testing system and dissatisfaction with results. Considerable variation in the tensile strength of supposedly comparable wounds has been found by investigators using different technics. The questions raised therein have been: Does this represent an error in technical measurement? Or is it a variation in healing? The answers involve consideration of the accuracy of the testing system and of the skill of the investigator in using it to maximum advantage. For example, the amount of friction and the steadiness of the pulling force over comparable periods of time are important factors in traction instruments. Furthermore, the wound must be properly aligned to avoid a shearing effect. The results with intra-abdominal distention technics have

been affected by variation in the size of the abdominal cavity. Rupture of pelvic peritoneum before the wound itself is another possible complication in wounds six days of age and older. It is beyond the scope of this paper to discuss in detail such features of tensile strength measurement. Our study was directed to the microscopic variables in midline laparotomy wounds of healthy rats which might affect such measurements. We shall consider first the stage of the skin cycle.

Description of cyclic changes in the hair follicles was reported in the rat in 1934 by Butcher [*1*]. Chase and his associates [*2,3*] described similar changes in mice and found variations in reaction to methylcholanthrene in different phases of the cycle. Wolbach [*10*] also pointed out that the reaction to carcinogenic hydrocarbons varied in different stages of the hair cycle in the mouse. Parnell [*5*], and Straus and Kligman [*8*] expanded their interests to other dermal structures and introduced the concept of the skin cycle. They thought that in rats, mice and rabbits the entire skin participated. Straus and Kligman [*8*] found variations in the spread of India ink in rabbits during different stages of the cycle. Straus, Kligman and Greenberg [*9*] reported that the reaction to radiation in mouse skin varied also. The resting hair was more resistant to the depilating effect of x-ray than the growing hair. Kligman [*4*] found that the susceptibility of the mouse, rat and hamster to ringworm infection was conditioned by the stage of the cycle. A period of susceptibility was found in the latter part of anagen. Radamacher and Montagna [*6*] believed that mouse skin reacted to the greatest degree to application of methyl ether of vitamin A and vitamin A palmitate, when the hair follicles were in the resting phase.

Although no studies have been described on the effect of skin cycles upon laparotomy wounds in rats, Randall and Randall [*7*] reported somewhat indefinite results on abrasive wounds in mice. They stated without elaboration that the effects of anagen and telogen were evident more in the degree of healing than in the presence or absence of healing.

We could obtain no correlation between the phase of the cycle and differences in degree of wound repair, the incidence of injury to skin appendages or the incidence of deep microscopic wound infection in the study reported herein. Since our series of wounds was relatively small in number, some reservation would appear justified before ruling out the skin cycle effect as a variable in wound healing experiments in the rat. Because of this uncertainty we have not included the variations in cycle encountered in our work among the total variables listed in our summary. Several means are available to eliminate it as a variable: plucking of hair in a given area initiates a new cycle [*8*]. If this procedure is applied to the proposed operative site as a preoperative measure, the animals can be placed in the same phase. Another possibility is the use of the guinea pig [*5*] which does not exhibit in all parts of a given area the same phase of growth as is the case in the rat, mouse or rabbit.

Many wounds in our series were complicated by deep microscopic infection or by involvement of injured skin appendages. With the special staining techniques used in this study local inhibition of both fibril deposition (reticulum) and fiber maturation (collagen) was observed in such complications. Moreover, positive Prussian blue reaction of the ground substance could be demonstrated by the Rinehart method in such areas. A positive reaction was normally found only in the stroma of the early stage of wound repair. The complication of deep infection might be avoided by wounding in a body area not as susceptible to mechanical irritation by the animal as the midline of the abdomen. In our current experimental work we are using the paravertebral shoulder area. The complication of injured skin appendages might be reduced by the use of hairless strains.

The step-shaped or shelf-like wounds described in a number of animals produced a more extensive area of scarring than resulted from precise vertical or perpendicular incisions. This effect on tensile strength is difficult to evaluate. The incidence of this variable might be reduced by increased awareness of this possibility on the part of the operator although the surgeon in this study attempted to make all wounds identical. Optimal operating conditions and factors such as proper light, anesthesia and animal relaxation hardly need to be mentioned.

Deep epithelial pockets containing keratinized material or exudate were sometimes observed. The base of such pockets led into the wound. The pocket was believed to result from lack of apposition and eversion of the upper part of the wound and subsequent epitheliza-

tion. The presence of exudate in the pocket was interpreted as evidence of infection. Serial section most probably would have indicated the source in a nearby level of the wound.

In some animals a wide, thin midline area was found with the rectus abdominis muscles separated to an abnormal degree. The diagonal wound shown in Figure 10 is such an example. It lay in a thin sling of fat and loose areolar tissue separated from the sheaths of the rectus abdominis muscle on each side. Such a wound could be expected to be less resistant to a test of rising intra-abdominal pressure than the one shown in Figure 5. Here the wound was buttressed by closely apposed rectus abdominis muscles and the wound margins were fused to the muscle sheaths. This variation was probably developmental. A relation might be considered also to factors such as the degree of apposition of wound margins and suture tension. It would seem unnecessary to stress the importance of careful selection of animals of uniform age, sex and weight in relation to this variable.

The wound involved muscle in a considerable number of animals. It was unavoidable whenever the superficial cutaneous maximus muscle crossed the midline. In others the incision inadvertently penetrated the sheath of the rectus abdominis muscle on one side or the other of the midline. The importance of this variable, and, to a much lesser extent, that of lymph nodules in the midline parietal peritoneum implicated by or abutting on the wound can only be estimated insofar as the effect on wound strength is concerned. It seems improbable that incised muscle and lymph nodules would heal at exactly the same rate as the preexisting collagen and fat in the linea alba and skin. In an attempt to minimize this variable we have restricted the depth of current experimental wounds to skin and subcutaneous fat only.

It should be emphasized before summarizing that the histologic variables listed in this paper are based on the findings in the mid-level only of the laparotomy wound. The number of variables most certainly would have increased if multiple blocks were taken, i.e., upper and lower poles as well as mid-level.

SUMMARY

Explanation was sought for variations which we experienced in the tensile strength values of comparable wounds. The variations could not be accounted for by the technique of measurement. Microscopic study was performed on "standardized" midline laparotomy wounds of thirty young adult male Wistar rats. We examined three groups of ten animals with wounds of seven, ten and fourteen days' duration. All wounds were made by the same operator. An additional group of ten animals was sacrificed without wounding and the midline anterior abdominal wall was studied microscopically.

Microscopic variations in transverse mid-level sections which might affect healing and tensile strength were found in twenty-six of thirty wounds and in four of ten specimens from the unwounded anterior abdominal wall. Suggestions are offered to minimize these variables.

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Lymphadenectomy via the Transperitoneal (Anterior Abdominal) Approach for Cancer of the Testis

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A PRIMARY consideration in the treatment of patients with malignant disease of many organs is the anatomic arrangement of their lymphatic systems. This is especially true of cancer of the testis, first, because of its strong tendency to metastasize via the lymph channels and, second, because excision of these structures presents exceptional problems. For these reasons opinion is divided, even among surgeons, as to whether or not lymphadenectomy should be attempted. Although all agree that the lymphatics should be treated, one group prefers roentgen therapy alone while another group, ourselves included, favors radical node dissection combined with radiation.

The technique of lymph node dissection for cancer of the testis has changed little since it was first described over half a century ago. The original retroperitoneal approach through a long flank incision is still in general use. Herein is reported a technique of lymphadenectomy performed via a midline abdominal or transperitoneal incision, which offers several advantages over the retroperitoneal route. Early studies relating to the testicular lymphatic system and evolution of the surgical treatment are reviewed as an introduction.

The lymphatic system of the testicle was described around the turn of the century by Horovitz and Zeissl [4], Most [6,7] and Cunéo [1]. Most, in 1898 and 1899 [6,7], and Jamieson and Dobson [5], in 1910, demonstrated the basic pattern by employing the technique of dye injection. They found that both the lymph and blood vessels passed out of the testis and over the psoas muscle to a point where the blood vessels cross the ureter. At this point, the lymphatics separated from the blood vessels and "sprayed themselves in graceful curves, fountain-wise, into the lumbar glands" [5]. The primary lymph nodes were the lumbar group located anterior and lateral to the aorta and vena cava below the level of the renal vein, together with one member of the external iliac group. Since the injected fluid passed from the testicle to the subclavian vein, these lumbar nodes constituted the sole barrier, although an imperfect one, between the testis and the thoracic duct. The cisterna chyli and the thoracic duct were quickly filled with the dye up to its termination in the vein [6,7].

Each testis had its own lymph system which communicated with each other and with those of adjacent structures. Jamieson and Dobson observed that the lymph vessels from the right testicle drained into lymph nodes lying anterior to as well as between the aorta and vena cava, and in the angle formed by the vena cava and the renal vein. An additional node was observed in the external iliac chain where the ureter crossed the artery. (Fig. 1.) The lymphatics of the left testicle drained into lymph nodes on the

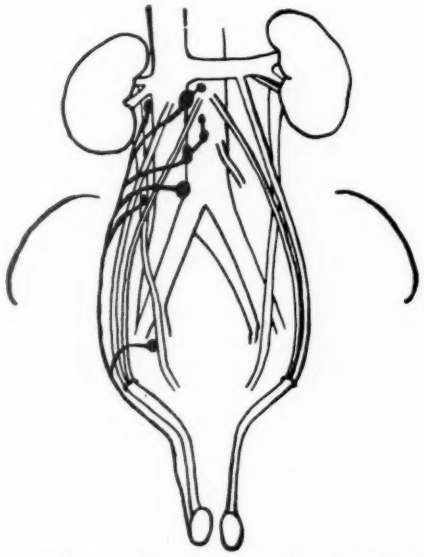

FIG. 1. Primary lymph nodes of the right testis.

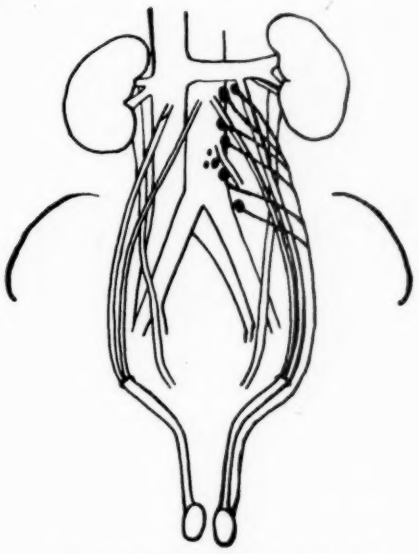

FIG. 2. Primary lymph nodes of the left testis.

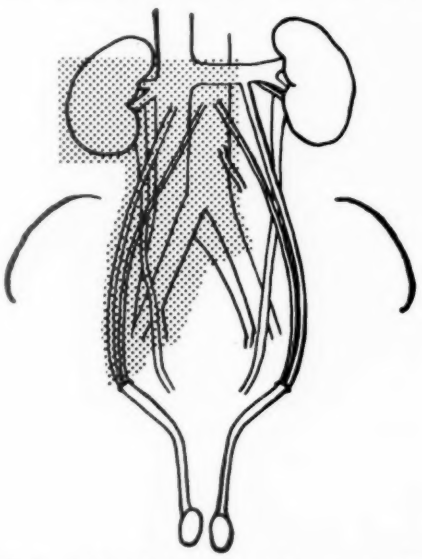

FIG. 3. Extent of node dissection for cancer of the right testis.

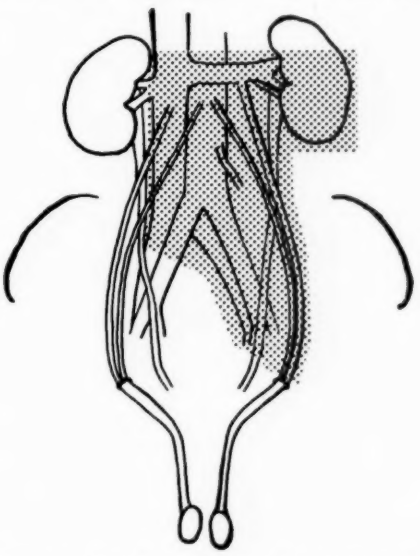

FIG. 4. Extent of node dissection for cancer of the left testis.

left side of the aorta from the renal vein down to the common iliac artery, particularly at the origin of the inferior mesenteric artery. (Fig. 2.) Secondary nodes were situated on the same and opposite sides, between and behind the aorta and vena cava, below and above the level of the renal veins, and along the outer side of each common iliac artery. These authors stated, "For surgical purposes, it is advisable to regard the glands as lying in various parts of the area bounded above by the renal veins, at the sides by lines drawn vertically a finger's breadth outside the vena cava and aorta, respectively, and prolonged to cross the external iliac arteries about the junction of the upper and middle thirds, below by lines drawn from the bifurcation of the aorta to meet the extremities of the vertical lines. The portions of the area containing the right and left glands overlap by the breadth of the aorta . . . the only effective method of removing the lumbar glands would be to strip the aorta and vena cava, the common iliac vessels, the proximal third or so of the external iliac vessels, the upper part of the spermatic vessels on either side, and the trunk of the inferior mesenteric artery, of all the cellulo-fatty tissue lying on, around, and in between them from the level of the renal vessels downward." (Figs. 3 and 4.)

Once the pattern of the lymphatic system of

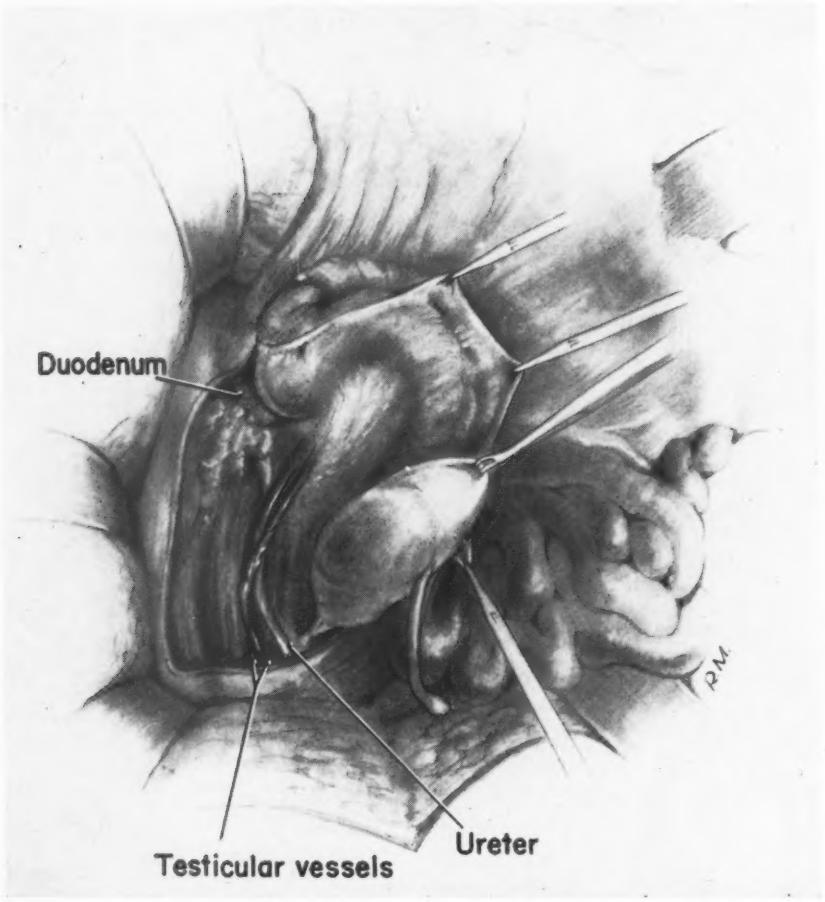

FIG. 5. Mobilization of the ascending colon.

the testis was established, surgeons became interested in a more radical approach to malignant disease of the organ. About 1900 European surgeons began to attempt excision of clinically palpable retroperitoneal masses, but without success. After a few years, however, the successful removal of clinically uninvolved lumbar nodes by the retroperitoneal route was reported by Cunéo and by Grégoire [3]. In 1901, Roberts [8] was apparently the first to undertake excision of clinically uninvolved lumbar nodes. The operation was performed through an abdominal, transperitoneal incision. This also seems to have been the first and only recorded use of the anterior approach. Intestinal obstruction and a fecal fistula developed and the patient died, presumably of peritonitis. The outcome of the case probably discouraged others, as well as Roberts, from undertaking further lymph node dissections by the anterior route.

By 1954, operations upon the abdominal aorta were being performed by a number of surgeons. For these procedures, a midline abdominal, or transperitoneal, incision was used routinely. In August 1954, in view of the difficulty of adequately exposing the lymph nodes in the region of the aorta and vena cava through a flank incision, one of us (J. S. S.) employed the anterior abdominal approach for radical lymph node dissection for carcinoma of the testicle. The success of the operation has led to its consistent use in our institution during the past year, and to the present time it has been performed upon sixteen patients.

TECHNIQUE

Prior to the operation, a Miller-Abbott tube is introduced under fluoroscopy. The long tube facilitates the handling of the small intestine at operation and reduces the possibility of subsequent partial obstruction. The procedure may be divided into four stages:

Stage I—Exposure of Retroperitoneal Space. The incision is made in the midline of the ab-

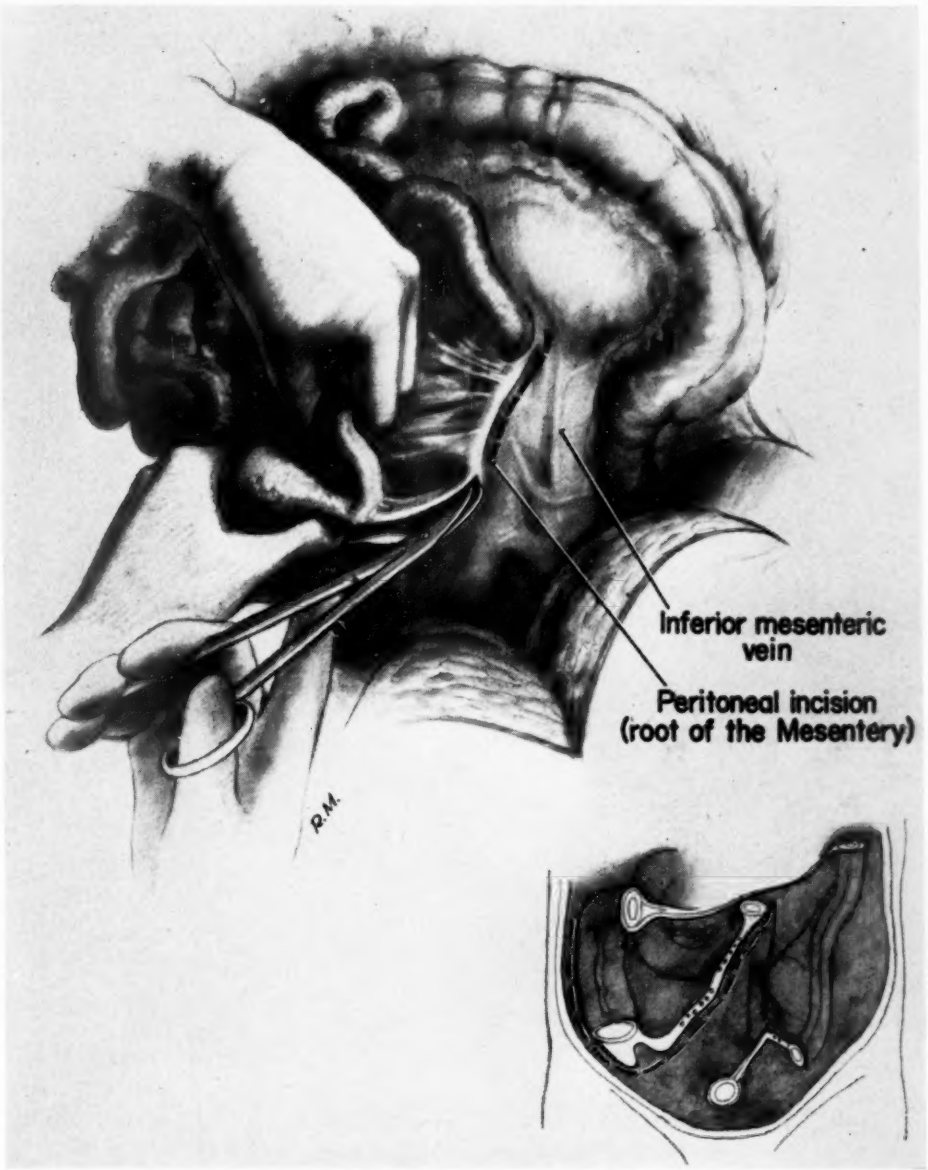

FIG. 6. Mobilization of small bowel with incision of peritoneum at root of mesentery.

domen from the xiphoid to the symphysis, and the abdomen is explored carefully for evidence of metastatic tumor. The area of the renal pedicle is particularly examined; if diseased nodes can be palpated above the renal vein, it is our opinion that the cancer cannot be completely excised and no lymph node dissection should be attempted.

The retroperitoneal space is exposed as described herein for cancer of either the right or left testis. This space is more accessible if the small bowel and cecum are removed from the abdominal cavity. To accomplish this, the ascending colon is first retracted toward the midline and the posterior parietal peritoneum is incised along the paracolic gutter. (Fig. 5.) Dissection is continued behind the colon through the avascular extraperitoneal connective tissue. With the cecum and small bowel elevated and retracted to the right, the peritoneal incision is carried in V-shaped fashion around the inferior border of the cecum and upward along the left leaf of the peritoneum at the root of the mesentery of the small bowel. This incision ends superiorly in the duodenal fossa between the duodenum on the right and the inferior mesenteric vein on the left. (Fig. 6.) The cecum and small bowel are then brought out, placed on the upper right abdominal wall and covered with warm packs.

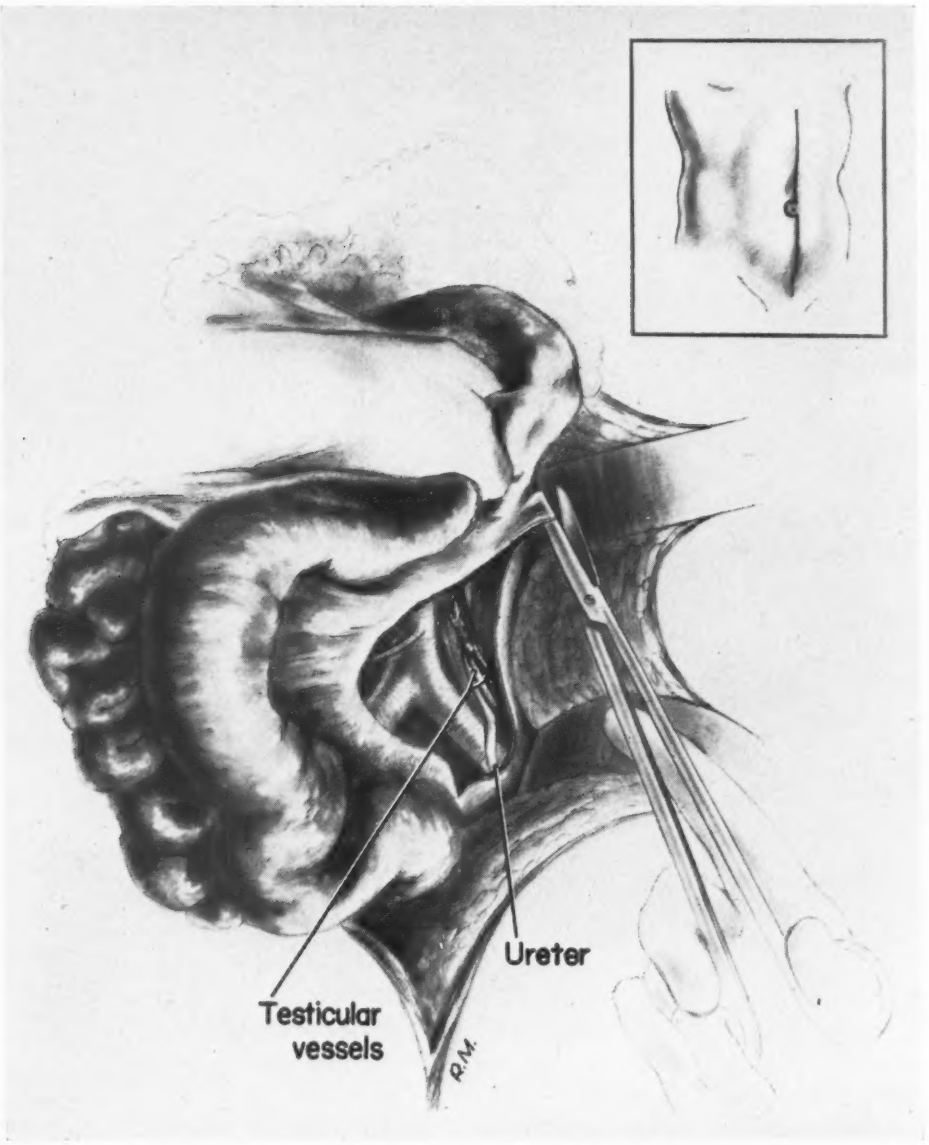

FIG. 7. Mobilization of descending colon.

Stage II—Lateral Dissection. The second stage consists of excision of the testicular blood and lymph vessels, dissection around the renal pedicle and removal of the lymph nodes in the lateral pocket. In cancer of the left testis, it is desirable to mobilize the ascending colon, the small bowel and descending colon, in this order; in cancer of the right testis, the ascending colon and small bowel are mobilized.

For removal of the lymphatics of the *left* testis, the descending colon is mobilized by incision of the posterior parietal peritoneum of the left paracolic gutter and the loose extraperitoneal connective tissue posteriorly. (Fig. 7.) The testicular vessels are identified and the vein is ligated at the level of the renal vein (vena cava on the right). The ureter, which usually adheres to the under surface of the peritoneum, is retracted with a rubber drain and freed superiorly and inferiorly with an intact thin layer of loose connective tissue. The testicular artery, vein and lymphatics are freed inferiorly to the internal inguinal ring, then ligated and divided at this site. The vas is ligated and divided where it descends behind the bladder. If the patient has previously had simple orchiectomy, the distal cut ends of the sutures on the vas and testicular vessels are left long in order to facilitate complete removal of this segment at the termination of the opera-

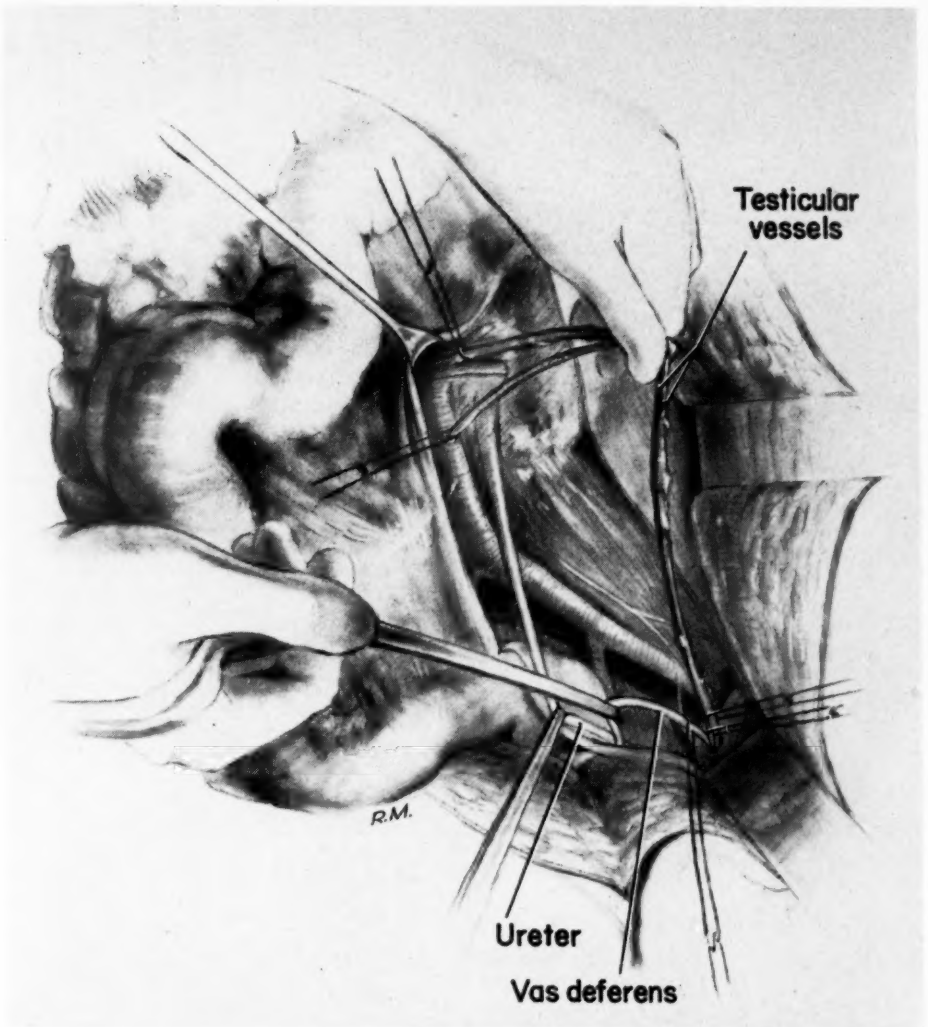

FIG. 8. Descending colon reflected, showing testicular vessels, ureter and vas deferens.

tion. The testicular vessels and lymphatics are freed upward and the fatty and loose areolar tissue is stripped from the anterior surface of the psoas muscle. The artery is ligated at the aorta. (Fig. 8.) The ureter is then traced upward to the hilum of the kidney. If exposure of the left kidney is difficult, the splenic flexure of the colon is mobilized. Once the ureteropelvic junction is visualized and the renal vein is clearly defined, the fascia and fat are stripped from around the convex border and posterior surface of the lower two-thirds of the kidney, leaving these tissues intact on the upper one-third. (Fig. 9.) The hilar dissection should be carried out with caution to prevent damage to the ureter, renal vein and accessory arteries. (Figs. 10 and 11.) The upper margin of the renal vein is exposed. The pocket formed by the testicular vein laterally, the left renal vein above, and the aorta medially is thoroughly cleansed of lymphatic and fatty tissue. (In operations upon the right side, these tissues are removed from the angle formed by the right renal vein and the vena cava.) These anatomic relationships are shown in Figure 12. The dissection is then carried medially to the opposite renal vein.

Stage III—Central Dissection. The central dissection is essentially the same for cancer of the right or left testis. It consists of stripping the aorta, vena cava and iliac vessels of their areolar, fatty and lymphatic tissues.

In order to mobilize the aorta and vena cava and open widely the intervening groove, the descending colon is retracted to the left, a retractor is placed behind the duodenum and

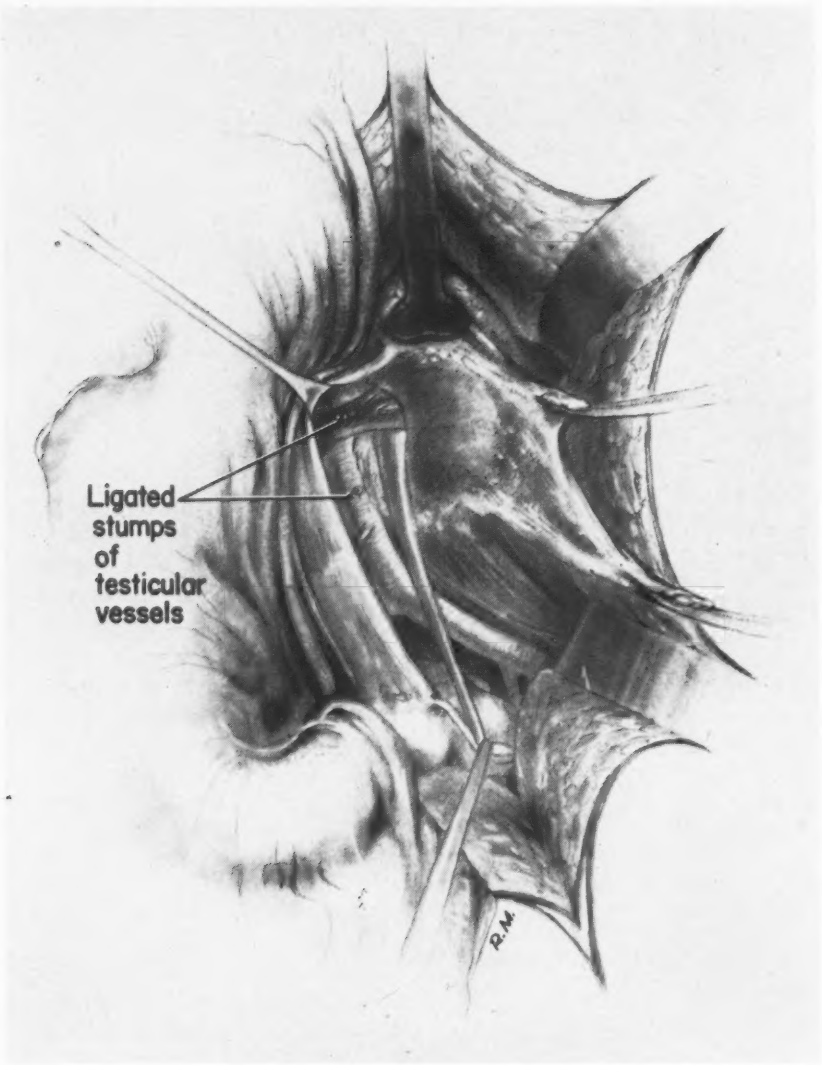

FIG. 9. Stripping of left kidney, renal vein visualized.

pancreas, and the lumbar vessels are ligated and divided. The upper portion of the central dissection is bounded above by the inferior margin of the left renal vein, on the right by the lateral border of the vena cava, and on the left by the lateral margin of the aorta. (Fig. 13.) The renal vein is gently retracted superiorly and the vena cava and aorta are retracted laterally. The lower portion of the cisterna chyli is clamped, divided and ligated. (Fig. 14.) At times, the cisterna lies at a somewhat higher level and cannot be visualized in the previously described pocket; in such cases, the major efferent lymphatic trunks are clamped, divided and ligated at the highest level. This thin-walled sac is easily injured and should be carefully handled; if injured it should be repaired, principally because of the possibility of disseminating viable tumor cells.*

With the descending colon still retracted to the left, the lymphatic, fatty and areolar tissue is stripped from the groove between the aorta and vena cava, as well as anteriorly, posteriorly and laterally to these vessels. The inferior mesenteric artery is identified about 4 cm. above the aortic bifurcation and is stripped downward to the origin of the left colic artery. The lymph nodes around the base of the inferior mesenteric artery lying in front of the aorta are likewise removed. The dissection is next pro-

* Perhaps it may be feasible to inject one of the chemotherapeutic drugs directly into the cisterna chyli. This has not yet been attempted although related experimental work is currently in progress.

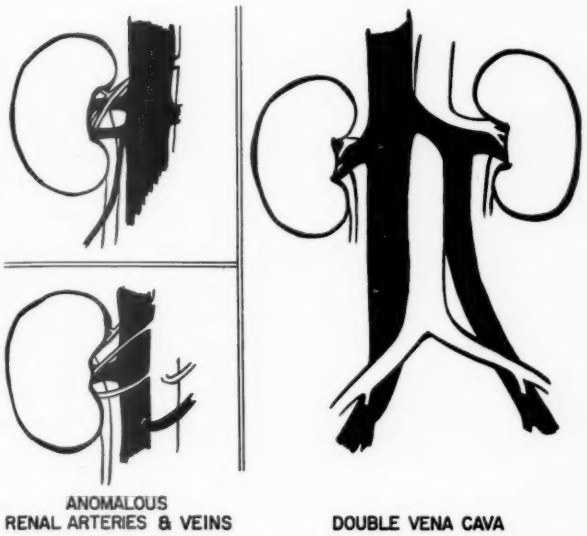

FIG. 10. Left, anomalous renal arteries and veins. Right, double vena cava.

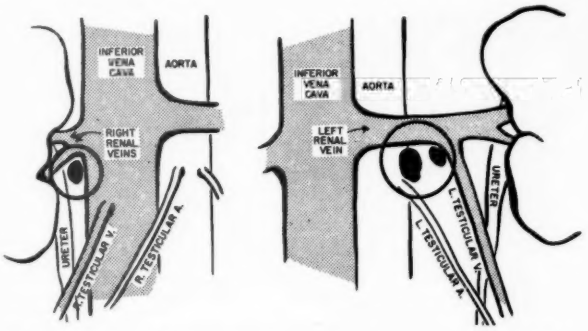

FIG. 12. Lateral lymphatic pockets, anatomic relationships.

longed downward along the iliac vessels, being facilitated by the insertion of tapes beneath the common and external iliac arteries. The lymphatics along these vessels are stripped down to the level of the inguinal ligament on the affected side and to just beyond the bifurcation of the iliac vessels on the unaffected side. The appendix is removed prophylactically. In our more recent cases we have been irrigating the retroperitoneal space with a 1 per cent solution of clorpactin (XCB) in an effort to destroy any loose tumor cells.

Stage IV—Peritoneal Closure and Excision of the Remaining Spermatic Cord. The cecum is returned to its normal position and sutured to the parietal peritoneum in the right lower quadrant. The peritoneum at the root of the mesentery of the small bowel is then closed with interrupted sutures of fine catgut. Careful closure of the duodenal fossa is important. This is accomplished by suturing the cut edge of the

FIG. 11. Double vena cava, rubber drain around aorta.

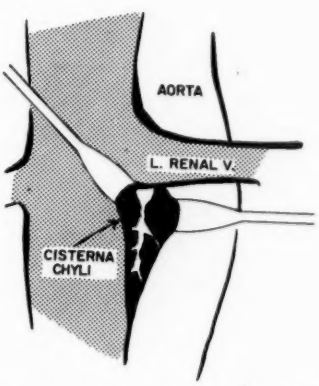

FIG. 13. Anatomic relationships, upper portion of central dissection.

peritoneum just medial to the inferior mesenteric vein to the wall of the duodenum itself. The paracolic gutter is left open. The wound is closed without drainage.

The vast majority of the patients who enter our hospital have undergone simple orchiectomy, in which most of the spermatic cord was left. In such cases, the remnant of cord is removed through a separate short inguinal incision. Following operation, routine care is administered. In none of the sixteen patients who have been operated upon by this approach have any significant complications developed.

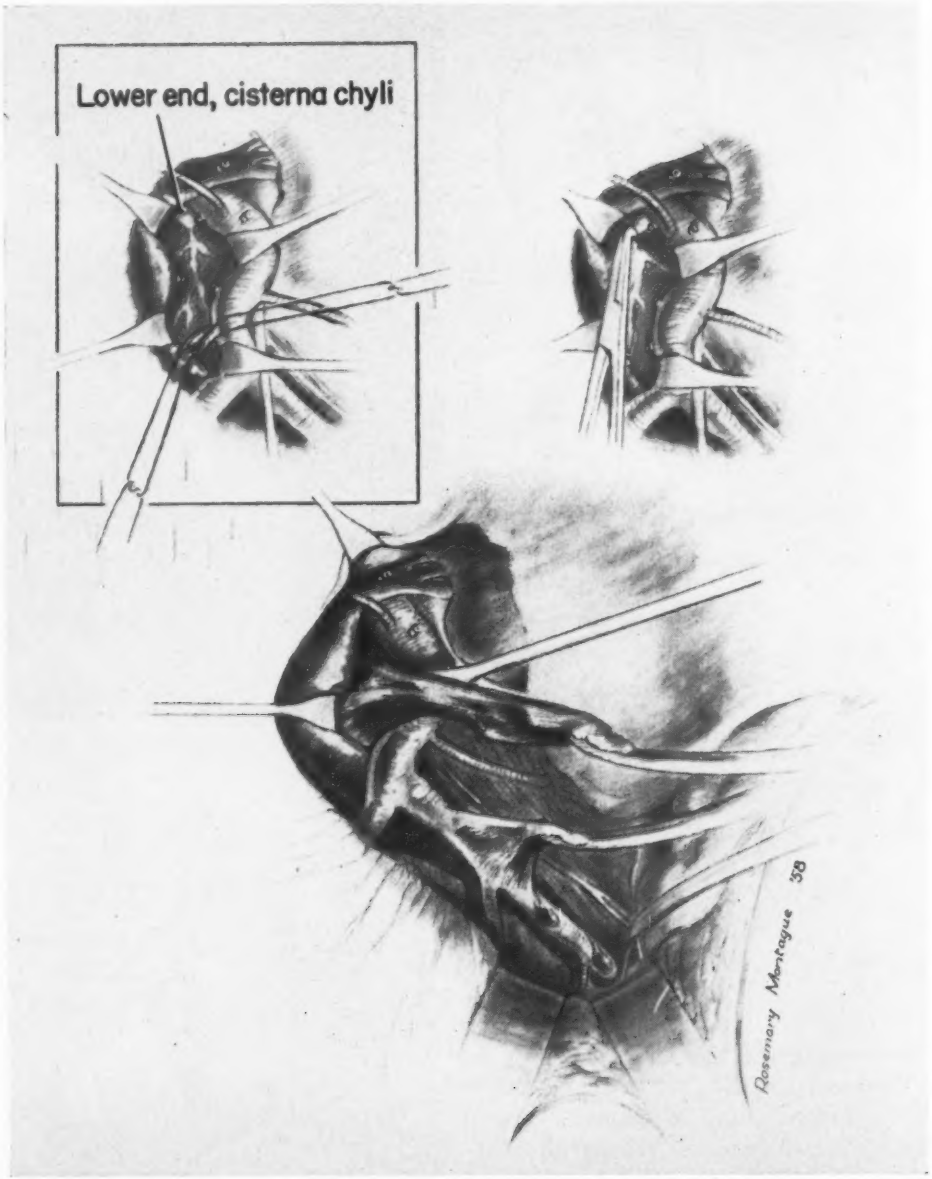

FIG. 14. Aorta and vena cava mobilized. Cisterna chyli ligated. Stripping of fatty, areolar and lymphatic tissue.

COMMENTS

The transperitoneal or anterior abdominal incision possesses several advantages over the retroperitoneal or flank approach for lymphadenectomy in cancer of the testicle. First, the exposure is simpler and more direct, and the necessity for dividing the abdominal muscles and nerves and opening the chest is thus avoided. More complete dissection of the lymph nodes around the aorta and vena cava and in the groove between these structures can be accomplished through the anterior approach, precluding any necessity for a second operation on the opposite side. In addition, because of better exposure, injury to these vessels, especially the veins, is less likely. If they are injured, however, the damage can be more easily repaired. We agree that a long flank incision which extends into the chest offers better exposure above the renal pedicle. If the disease has obviously extended above this point, however, we believe that dissection should not be undertaken. It is doubtful that any patient with gross tumor above the pedicle will be salvaged because of the location of the cisterna chyli and the thoracic duct.

One of the reasons for an unsuccessful outcome following node dissection for cancer is the dissemination and implantation of malignant cells during the procedure. The possibility of this complication is perhaps greater in node dissection for cancer of the testicle than for cancer in other locations. These lymphatic structures do not lend themselves readily to *en bloc* dissection; first, they are strung out over a considerable distance from the testis and, second, they have no protective cushions of fat, fascia and muscle, as is generally true of the nodes in the neck, axilla and groin. As a consequence, if they contain viable tumor cells, implantation is probably more likely than in node dissections in the latter regions. The danger of dissemination and implantation may be minimized, however, by observance of the following precautions: (1) gentle clinical examination of the primary lesion; (2) extreme care in handling the tissues during the operation and preliminary ligation of the testicular vein; and (3) irrigation of the wound at the conclusion of the procedure to remove or destroy loose tumor cells. If simple orchiectomy has been performed previously, roentgen therapy to the affected groin and lymph node area with the cobalt 60 unit prior to dissection will serve as a further precautionary measure against spread of the disease.

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The Anterolateral Approach to the Upper Cervical Vertebrae

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LESIONS of the bodies of the upper cervical vertebrae occasionally present difficulties in diagnosis and therapy. Tissue removed for pathological examination often yields a rapid and certain answer while other indirect diagnostic tests may leave much room for conjecture. It is the purpose of this paper to present the anatomical features which make examination of tissue feasible. Although our experience has not been extensive, it is believed that by careful attention to anatomical landmarks, open biopsies in this region can be made a quick and safe procedure. While it is not the purpose of this paper to discuss the relative merits of open versus needle biopsy, it is to be noted that detailed descriptions and case reports of needle biopsies of the upper cervical vertebrae are infrequent. A recent paper by Craig [1] on the details of needle biopsies uses for its case reports only biopsies of the thoracic and lumbar vertebrae.

The pharyngeal approach to the upper cervical vertebrae has been mentioned by several authors [2–4[. Valls et al. state, "the body of the axis and the third cervical vertebra are hardly accessible to palpation. Since they are deeply placed in connection with the organs of the neck, it is advisable to find them by the pharyngeal route" [4]. No details of the pharyngeal approach are given. A great deal of support for this approach is taken from the fact that abscesses of the retropharyngeal area have been drained via this pharyngeal approach for many years.

Southwick and Robinson suggest that the upper cervical vertebrae can best be reached by a pharyngeal approach [2]. In a case which was presented in detail, an osteoma of the second and third cervical vertebrae was removed in this fashion; however, tracheostomy was required postoperatively.

It is our opinion that there are essential differences in approach to the patient with an infected retropharyngeal abscess as compared to the patient with a non-infectious bony pathologic condition of the upper cervical spine. We believe that the transpharyngeal approach is fraught with dangers of infection and uncontrollable hemorrhage, in addition to anesthetic and postoperative pulmonary difficulties.

The anterolateral approach to the deep structures of the neck is relatively well known. Lahey [6] has described its use in resection of cervical esophageal diverticula and the paper by Southwick and Robinson [2] gives an excellent description of the anterolateral approach to the lower cervical spine. Kulowski [5] recommends an anterolateral approach for drainage of a retropharyngeal abscess but details are not given.

We shall present the anatomical details of an anterolateral approach to the upper cervical vertebrae. It might be mentioned that some experienced surgeons [3] advocate an approach posterior to the sternocleidomastoid muscle for the lower cervical vertebrae. It is our belief that such an approach is not feasible when dealing with the upper cervical vertebrae.

ANATOMICAL LANDMARKS TO THE ANTEROLATERAL APPROACH TO C2–4

A transverse skin incision is made about 1 to 2 fingerbreadths below the angle of the mandible depending upon the exact vertebra in question. Two-thirds of the incision should lie anterior to the anterior belly of the sternocleidomastoid muscle and one-third of the

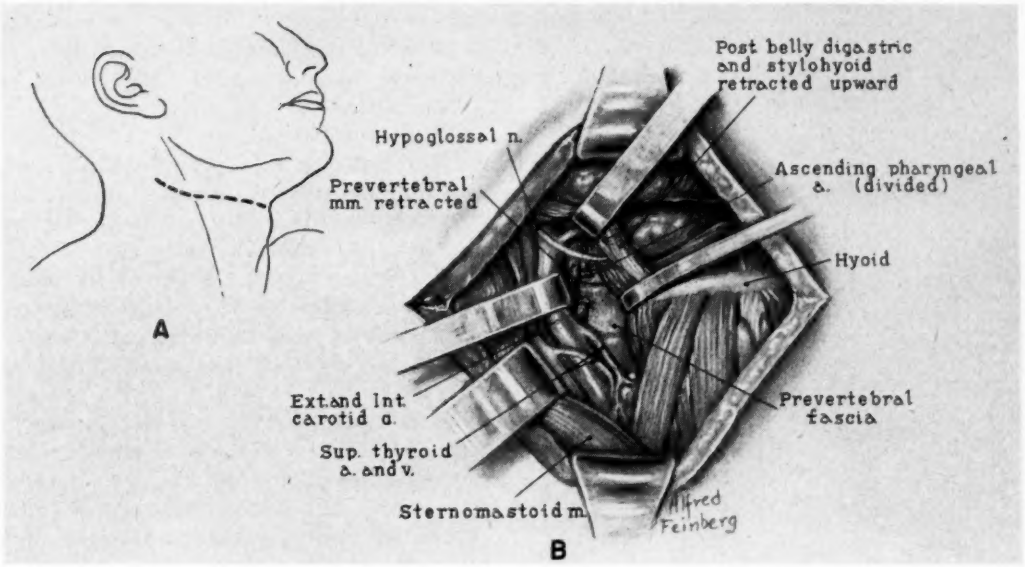

FIG. 1. A, transverse skin incision. B, details of operative site.

length of the incision should lie posterior to it. The subcutaneous tissue and platysma are divided in a similar fashion. It is best to carry out this latter dissection somewhat toward the inferior skin margin so as to avoid the tip of the parotid gland and the mandibular branch of the facial nerve when the dissection is carried deeper. The fascia investing the anterior border of the sternocleidomastoid muscle is divided in a vertical direction. At this point tributaries of the posterior facial vein and posterior superficial jugular vein may be encountered. The posterior belly of the digastric muscle is then identified in conjunction with the stylohyoid muscle. As the stylohyoid muscle and posterior belly of the digastric muscle are retracted superiorly, the hypoglossal nerve can be readily identified crossing the operative field in a transverse direction. Directly beneath the hypoglossal nerve lie the internal and external carotid arteries. The carotid arteries can then be gently retracted in a lateral direction thus giving access to the prevertebral muscles. The ascending pharyngeal artery may become visible at this point. Its position is not constant, but an attempt should be made to identify, divide and ligate it. The ascending pharyngeal artery arises as the second branch of the external carotid artery, but it may be the first. Its size is inconstant depending upon the size of the ascending palatine vessels. It runs in a superior direction towards the base of the skull traversing the field of dissection in a vertical fashion. Bleeding may be severe if this artery is not controlled. (Fig. 1.)

We have now reached the muscles lying on the anterior surface of the vertebral column. The vertebral bodies are covered by the muscular and aponeurotic fibers of the longus capitus and longus colli muscles. By staying in the midline, it is a simple matter to separate these fibers by blunt dissection thus exposing the anterior surface of the bodies of the second, third and fourth cervical vertebrae. Keeping the dissection in the midline avoids the dangers of interrupting the cervical sympathetic chain and also prevents injury to the vertebral artery when an attempt is made to take a biopsy specimen of bone in this area. (Fig. 2.)

The exact identification of the vertebral body can be checked by x-ray control. However, if the tip of the cornu of the hyoid bone

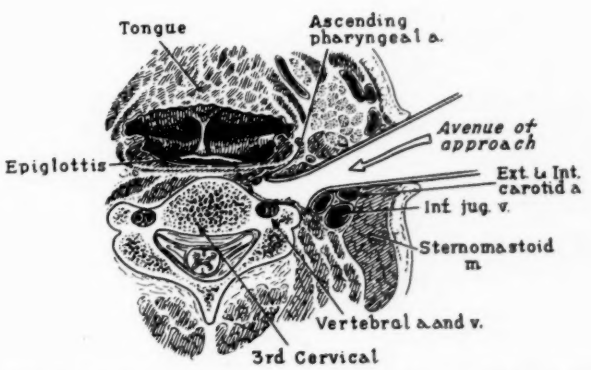

FIG. 2. Cross sectional view of avenue of approach to the anterior surface of the third cervical vertebra.

FIG. 3. X-ray evidence of destruction of body and right transverse process of third cervical vertebra (arrow).

is palpated and an imaginary line is drawn directly posteriorly, it will coincide with the level of the third cervical vertebra. By extending the dissection in the midline superiorly and inferiorly, the second and fourth cervical vertebrae can be exposed respectively.

CASE REPORT

CASE 1. C. B., a twelve year old Negro boy, was admitted to Babies Hospital because of pain in the neck of five months' duration. The patient was in apparent good health until five months prior to admission when he had an insidious onset of pain and stiffness in the neck. The pain progressed in severity. After one month, he had a fixed torticollis with the neck held toward the left and the chin turned toward the right. The pain increased in severity and five days prior to admission he had an episode of nausea, vomiting and diarrhea.

Physical examination showed that the chin was held to the right. The range of motion of the cervical spine was limited in all directions due to pain. There was no specific involvement of the nerve root. The remainder of the physical examination was not remarkable. X-ray films disclosed extensive destruction in the third segment of the cervical spine. (Fig. 3.) This destruction involved largely the right transverse process and a short segment of the body on the right side. The intervertebral space between C2 and C3 had been obliterated.

While the patient was in the hospital signs of increased intracranial pressure developed necessitating a ventriculopleural anastomosis. The patient had to be kept in head traction during this time to avoid possible injury to the spinal cord.

On September 9, 1957 under endotracheal anesthesia, Crutchfield tongs were inserted and a biopsy specimen of the third cervical vertebra obtained through the previously described anterolateral approach.

Pathological examination documented the presence of a histiocytoma. Postoperatively the patient did well. There was mild edema of the posterior pharyngeal wall. A small bore nasogastric tube was passed for feeding purposes. It was removed after several days. The wound healed per primam. At no time was there any respiratory distress. There was transitory weakness of the right hypoglossal nerve. The patient was started on radiotherapy with some alleviation of symptoms.

SUMMARY

1. The anatomical landmarks for a safe open approach to the second, third and fourth cervical vertebrae have been outlined.

2. The advantages of the anterolateral approach over the transpharyngeal are presented.

5. A case history is reported illustrating the merits of this procedure.

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CASE REPORTS

Conservative Management of Eventration in the Newborn, with Survival

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EVENTRATION in the newborn is an extremely formidable condition, and differs from a simple omphalocele in that with eventration there is a huge anterior defect in the abdominal wall and the abdominal cavity is very small. This striking inadequacy in the size of the abdominal cavity forces the viscera—the bowel, liver and stomach—into the huge extra-abdominal omphalocele sac [*1,2*].

Surgical closure should not be attempted early, but often the covering is ruptured at birth and there seems to be no other alternative. However, because it is a rare entity (about 1 per 10,000 births) and reportedly almost 100 per cent incompatible with life, surgical attempts at closure have been considered the logical approach [*1,2*]. Since there is such marked inadequacy of the abdominal cavity, such efforts at surgical closure lead to severe compression and occasionally to gangrene of enclosed viscera thus hastening the death of the infant. There have been only a few authors [3] who have advocated conservative management, since these babies usually die within five or six days of necrosis, fatal peritonitis or rupture of the covering.

In the simple omphalocele [*4*] there is a wall defect of lesser degree, with a normal-sized abdominal cavity and only a few loops of bowel to replace. Accepted treatment has been to close these surgically in the first twelve hours if possible, taking advantage of the period of high neonatal resistance to trauma and the relatively clean field.

On January 22, 1958, we were called to see a newborn female who had been delivered at full term with an eventration which included most of the small bowel, the liver and part of the stomach. The covering membrane (evidently the wall of the umbilical cord), although tissue-paper thin, was intact. The body circumference just below the extrusion was 10 inches which indicates the degree of maldevelopment of the abdominal cavity.

The situation was considered hopeless as surgical treatment seemed impossible. However, to protect the delicate covering membrane, we decided to find a soft, non-adhering material. Klear-Vu,* a polyethylene film used to enclose commercial articles, was chosen because of its non-adhering and non-irritating qualities. This film was cut into sheets adequate to cover the mass. These were sterilized in 1:1000 Zephiran® solution. The outer dressing consisted of a ring of cotton around the base of the mass with an overlying cotton pad and binder. Daily changes were made. As prophylaxis against infection, the infant was given 0.25 gm. of dihydrostreptomycin and 200,000 units of procaine penicillin G intramuscularly daily for the first week.

To our amazement, this treatment proved that conservative management could be effective. By the tenth day the membrane was clean, odor-free, was beginning to thicken and was becoming opaque.

Feeding was carried out very cautiously, starting with a dropper, then small bottle feedings of powdered similac, ranging from 1:4 down to standard dilution by the second week. The course was gratifyingly steady and uneventful.

When we saw the baby doing so well, the mother was trained in the dressing technique, and the

* Klear-Vu, manufactured by the Klear-Vu Corporation, New York 3, New York. It is easily obtained from central supply of most hospitals as it is widely used. It cannot be autoclaved.

FIG. 1. Age six days (Jan. 28, 1958).

FIG. 2. Age four weeks (Feb. 20, 1958). Note developing cuff of skin.

FIG. 3. Age seven weeks (March 13, 1958).

FIG. 4. Age ten weeks (April 3, 1958).

FIG. 5. Age twenty weeks (June 10, 1958).

FIG. 6. Age twenty-seven weeks (July 31, 1958).

infant sent home at two weeks of age, with a visiting nurse who had been thoroughly briefed to aid for a few days. Since that time the mother has given excellent care and the feedings have progressed normally.

At birth this baby weighed 5 pounds 8 ounces; at six weeks her weight was 7 pounds 4 ounces; at two and a half months, 9 pounds 5 ounces; and at four and a half months, 12 pounds. The abdominal circumference, from 10 inches at birth, increased to 11½ inches at six weeks, to 13 inches at two and a half months, and to 15 inches at four and a half months.

The photographic sequence (Figs. 1 through 6) shows graphically that conservative management can be far more logical and immeasurably safer than radical surgery for the infant with this condition, especially when we are aware of the fact that incompatibility with life has been the gruesome label heretofore.

May we conclude by re-emphasizing the extreme importance of not risking almost certain surgical failure without carefully evaluating the possibility that conservative measures may be not only far better but will be less hazardous to the infant, and so will add one more factor to improve neonatal mortality.

We were especially grateful for this opportunity to help save this particular baby, as she represented the first pregnancy for a couple who for thirteen years had had a barren marriage.

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Congenital Esophageal Stenosis

PATHOLOGIC STUDIES FOLLOWING RESECTION

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In contrast to esophageal atresia with tracheoesophageal fistula which is a true surgical emergency requiring immediate operation, congenital esophageal stenosis is compatible with life and may not be recognized until childhood. The true incidence of this condition is not well established since many mild cases may go unrecognized, attention being focused on repeated respiratory tract infections and regurgitation, many cases being interpreted as normal feeding problems in the young. Prior to 1943 when Haight first performed a successful one-stage resection for esophageal atresia, the only available treatment for esophageal stenosis consisted of esophageal dilatation. With the advent of antibiotics and improved techniques for intrathoracic surgery, case reports appeared in the literature, end-to-end anastomosis of the esophagus having been carried out successfully with excellent relief of symptoms [*1,4,5,7*].

Congenital obstruction of the esophagus is a developmental abnormality following failure of recanalization of the trachea and esophagus into structures of adequate lumen. In the third to twelfth week of fetal life the trachea and esophagus are a single primordial tube which later becomes obliterated with epithelial proliferation. Muscular ingrowth separates this tube into two distinct longitudinal portions which later vacuolize and coalesce to form the distinct lumen. Abnormalities of development may appear as short segmental webs resembling a mucosal diaphragm, or as a narrowed segment of the esophagus varying in length from 2 to 15 mm. Multiple stenotic segments have been reported. The association of esophageal stenosis with tracheoesophageal fistula can be explained by abnormal joining of the esophagus and trachea during this developmental period.

The most common symptom occurring in these infants is that of regurgitation particularly when solid food is added to the diet. Forceful vomiting rarely is seen as the proximal portion of the esophagus becomes dilated and a passive regurgitation results following food intake. The regurgitated fluid resembles undigested formula and rarely contains bile-stained material. Aspiration and secondary infection of the respiratory tract frequently occur secondary to this phenomenon. Failure to gain weight is common. In near complete stenosis of the esophagus the diagnosis is made earlier because of the severity of symptoms; however, in the milder case marked dilatation and hypertrophy of the entire proximal esophagus may occur prior to the discovery of the condition. Associated gastrointestinal abnormalities were found in 12 per cent of cases in one series [*7*]. The roentgenographic diagnosis is not usually difficult once the condition is suspected clinically. A small catheter is placed in the proximal segment of the esophagus and slow instillation of a water soluble radiopaque medium is carried out to outline the stenotic area [*5*]. Fifty per cent of obstructions were found to occur in the middle third of the esophagus and in this area were usually of the segmental variety. The distal third of the esophagus is the more common area for the occurrence of congenital web type obstruction.

Until recently the recommended treatment for congenital esophageal stenosis was dilatation, either through an esophagoscope or bouginage with dilators passed over a swallowed string guide [*7*]. Gastrostomy was necessary at times to allow for retrograde bouginage which was considered safer than either of these two methods [*10*]. In recent years, however, patients

FIG. 1. Preoperative roentgenogram shows segmental stenosis of the middle third of the esophagus in a five month old male infant. Rather marked dilatation of the proximal esophagus is already evident.

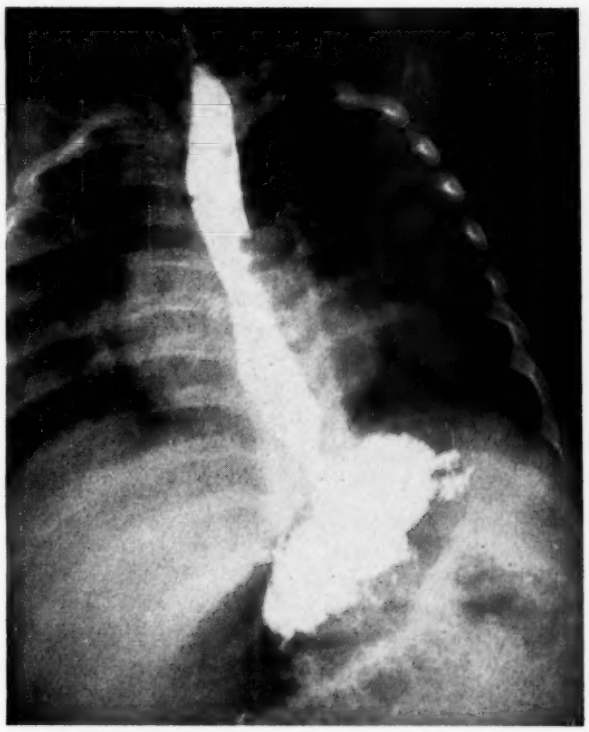

FIG. 2. Postoperative barium swallow on the ninth day demonstrates excellent caliber without narrowing at the site of end-to-end anastomosis. Although the esophageal diaphragmatic hiatus was dilated at operation to assist in attaining length for tension-free suture, this film shows all of the stomach to be well below the diaphragm.

have been followed up after primary resection with anastomosis of the esophagus and have shown lasting excellent results. The type and severity of the obstruction should be considered in outlining therapy for segmental obstruction of near complete obliteration of the esophageal lumen. Dilatations should not be expected to bring about cure and occasionally are associated with severe complications. With failure to gain weight or repeated aspirations and infection of the upper respiratory tract, operation is indicated. Failure to respond to esophageal dilatation also should be considered as an indication for surgical excision. A right thoracotomy approach transpleurally with resection and end-to-end anastomosis of the esophagus is recommended. Anastomosis should be made without tension which may necessitate freeing up of the distal and proximal ends of the esophagus and at times enlarging the esophageal hiatus, delivering the stomach into the thorax. The use of Pott's arterial clamps may help in relieving tension on the suture line during the performance of the anastomosis. Single or double layer interrupted silk sutures or other non-absorbable material are advocated. The thorax should be closed with under-water-seal drainage during the immediate postoperative period. A splinting catheter should not be placed across the anastomotic line in the esophagus since this favors tissue breakdown and hinders the normal swallowing of saliva so that aspiration and pulmonary infection may result. A temporary Stamm gastrostomy is recommended for feeding during the initial postoperative period. A thin barium meal may be given on or about the tenth postoperative day and if the anastomotic line is of sufficient caliber oral feedings may be started. The child should be placed in a semi-upright position to help with gravity flow to the esophagus and stomach. The phrenic nerve should not be divided in infants since respiratory excursion is important in preventing postoperative atelectasis and pneumonitis. Similarly, the vagus nerves should be identified and spared. On occasions, dilatations have been required following end-to-end anastomosis of the esophagus but usually are unnecessary [*11*].

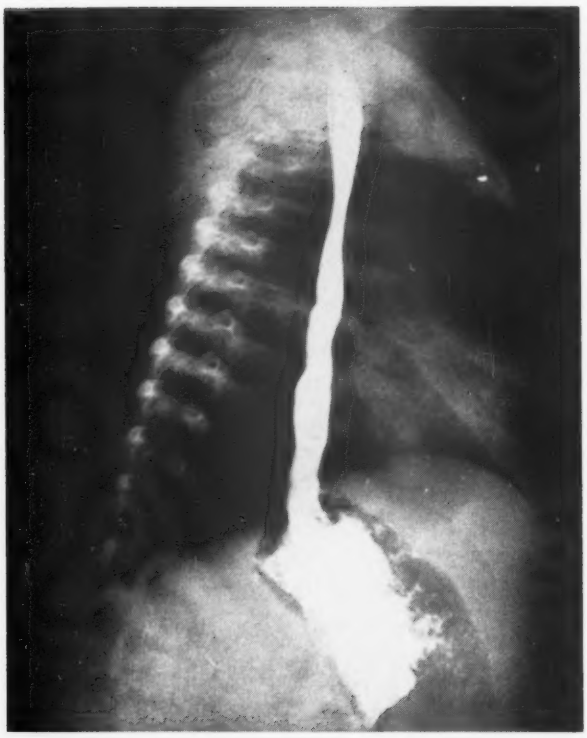

FIG. 3. A lateral view six weeks after operation shows excellent caliber of lumen with almost complete resolution of the proximal dilatation originally seen.

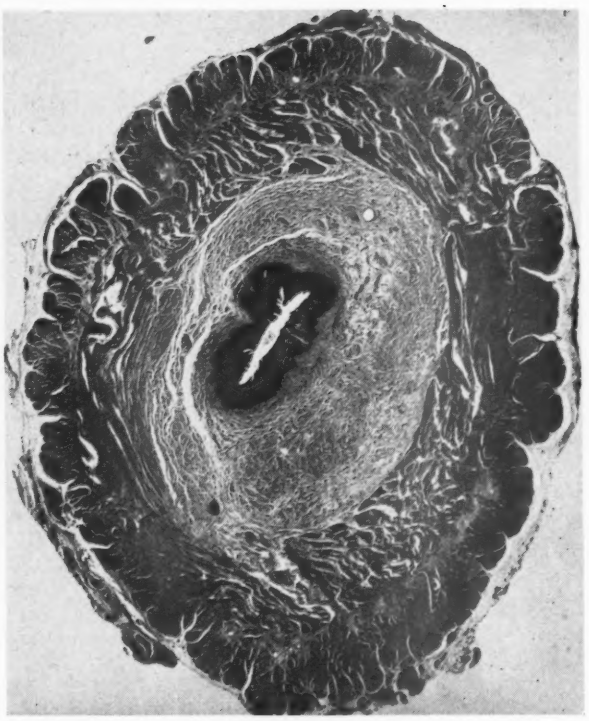

FIG. 4. Microscopic section at the site of stenosis shows the extensive submucosal fibrosis and thickening by smooth muscle fibers which almost form a third but ineffectual muscle layer. The mucosa is not thrown into folds and dilatation would have been a very slow process attended by some trauma and additional fibrosis.

CASE REPORT

A five month old white male infant entered Tripler United States Army Hospital with a history of poor weight gain and frequent infections of the respiratory tract since the age of two weeks. The pregnancy and neonatal period were uneventful until the onset of this illness. When oral feedings were started the child had some difficulty with abundant accumulations of saliva and mucus within the pharynx and upper respiratory tract. From eight to ten feedings were required daily with the majority of the formula being regurgitated shortly after ingestion. The child had been hospitalized on two occasions prior to this admission because of pneumonitis and bronchiolitis secondary to aspiration. Physical examination on admission disclosed a thin, poorly nourished child appearing younger than the stated age of five months, weighing 11 pounds, 9 ounces. The rectal temperature was normal. Both lung fields contained coarse rales with inspiratory and expiratory rhonchi present in both bases. The remainder of the physical examination was entirely within normal limits. No associated congenital abnormalities were demonstrated.

X-ray examination of the chest revealed increased lung markings in the perihilar region of both lung fields with no evidence of consolidation or pneumonitis. An upper gastrointestinal study using water soluble opaque medium demonstrated a segmental type of esophageal stenosis in the middle third approximately 1.5 cm. in length, associated with marked dilatation of the proximal esophagus. (Fig. 1.) No associated fistulas were seen. Routine laboratory work was within normal limits.

Under general anesthesia right thoracotomy was performed (W. F. B.) with transpleural approach to the esophagus, dividing the azygos vein. The stenotic portion which measured approximately 1.5 cm. in length was excised. Of interest is that the outward appearance of the stenotic area was of a normal diameter. With a small soft rubber catheter in place to the site of obstruction, resection was carried out until a normal lumen was visualized proximally and distally. Utilizing Pott's arterial clamp and freeing up of the distal and proximal parts of the esophagus in the area, anastomosis was carried out without tension

using a single layer of interrupted 4-0 silk sutures. Stamm gastrostomy was performed at the time of surgery. Antibiotic coverage was utilized both prior to and following operation because of the increased risk of pneumonitis.

On the ninth postoperative day radiographic studies revealed a satisfactory lumen at the site of anastomosis and oral feedings were started. (Fig. 2.) The child took these well and occasionally had regurgitation problems if fed in the supine position. However, with Fowler's position utilized during feeding no regurgitation was noted. General improvement in physical condition and steady weight gain followed operation. (Fig. 3.)

Pathologic examination of the resected specimen disclosed a lumen measuring less than 2 mm. in diameter surrounded by a ring of firm, grayish yellow tissue consisting of thickened submucosa composed of loose fibrous connective tissue and abundant muscle bundles occupying almost the entire submucosal area in some areas. The circular and longitudinal layers of the muscularis were slightly thickened. Normal nerve fiber bundles and ganglion cells were identified in the resected tissue between the layers of muscles. The mucosal surface at the point of stenosis was composed of a fairly thick uniform layer of stratified squamous epithelium which was unremarkable. (Fig. 4.)

COMMENTS

This patient represents a case of congenital segmental esophageal stenosis involving the middle third of the esophagus in whom dilatations and bouginage would have offered little relief. Resection of the involved segment with end-to-end anastomosis of the esophagus are carried out with excellent postoperative results and with little postoperative morbidity. All degrees of stenosis of the esophagus may be encountered in infants. However, when near complete obstruction to the lumen is discovered with associated lack of normal weight gain and repeated aspiration pneumonias, surgical resection should be carried out. However, web-like stenosis of the esophagus usually responds well to esophagoscopy and bouginage, and resection of involved segments is rarely indicated. With better techniques for intrathoracic surgery in infants and the use of antibiotics for additional protection against postoperative pulmonary complications, surgical treatment for esophageal stenosis should be recommended when these conditions are met.

Examination of the specimen by the pathologist disclosed normal nerve tissue and ganglion cells. The apparent pathologic process consisted of abundant smooth muscle tissue and fibrous connective tissue with a thickened poorly organized submucosal layer of the esophagus. No inflammatory process was seen and the mucosal surface of the involved segment was normal. This hypertrophy of muscle layer and fibrosis has been described in previous papers in which pathologic examination has been carried out on resected specimens [5]. Relief could not be expected following transesophageal dilatation.

SUMMARY

1. Congenital esophageal stenosis is not a surgical emergency and is compatible with life, symptoms varying with the severity of the condition.

2. Common symptoms are those of passive regurgitation of ingested material with history of repeated infections of the respiratory tract and poor weight gain.

3. Esophageal stenosis may be web-like consisting of a mucosal diaphragm in the distal third of the esophagus or may be segmental, typically in the middle third of the esophagus, associated with submucosal and muscularis thickening with fibrosis and hypertrophy.

4. Indications for surgical resection include failure to respond to esophageal dilatation, hypertrophy and dilatation of the proximal esophagus with regurgitation and aspiration, repeated infections of the respiratory tract secondary to aspiration, and poor weight gain or malnutrition.

5. The right thoracotomy approach with division of the azygos vein is recommended with resection of the involved segment and end-to-end anastomosis utilizing interrupted non-absorbable sutures. Gastrostomy should be used during the immediate postoperative period for feeding purposes.

6. A case report of segmental congenital esophageal stenosis is included in which surgical treatment was carried out with satisfactory postoperative results.

7. Pathologic examination of the resected tissue revealed submucosal changes of fibrosis and disorganized smooth muscle fibers with normal nerve tissue present.

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The National Health Education Committee said in a report entitled "What Recent Research Progress Against Cancer?" that sixteen chemical compounds that produce temporary improvements in patients afflicted with various forms of malignancy have been discovered. The survey also found that another ten chemicals have exhibited cancer-fighting possibilities. More than 42,000 compounds were screened by government and private agencies. New diagnostic technics are also being used with good results. Unfortunately, many people wait too long before consulting a physician, with the result that each year 42,500 Americans die needlessly.

Voluntary Bilateral Posterior Dislocation of the Shoulder Joint

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VOLUNTARY dislocation of the shoulder joint is a rare phenomenon. Reischauer [*6*], in his comprehensive review of the subject, classified the condition into three types: (1) purely voluntary luxation, (2) habitual-voluntary luxation, and (3) pendulum luxation.

The essential characteristics of the first type are that the dislocation at no time occurs involuntarily, even during severe exertion, that there is no uncertainty or insecurity in the use of the limb and that the patient suffers no pain or disability. No pathological features are seen in the shoulder joint or in neighboring structures.

Habitual-voluntary dislocation is that which is seen in patients suffering from habitual or recurrent dislocation of the shoulder. It is well recognized that some such patients develop the ability to dislocate the joint voluntarily, the joint continuing to luxate involuntarily as well. Most of these instances follow an initial traumatic dislocation and are frequently associated with a pathological condition of the joint or its surrounding structures.

Pendulum luxation is that which occurs when a specific movement, e.g., abduction, is voluntarily or involuntarily performed; when the arm is restored to its original position, the luxation automatically reduces itself.

Reischauer [*6*] was able to gather ten definite and two doubtful cases of purely voluntarily dislocation from the literature. We have been able to trace reports of six cases of voluntary dislocation published since Reischauer's review. Three of these are of the habitual-voluntary type [*1,8,10*] and the other three [*12*] probably fall into the purely voluntary category although pain and disability were present. In view of the rarity of purely voluntary dislocation and because we have found no similar description of this condition in the English literature, a report of the present case was considered worthwhile.

CASE REPORT

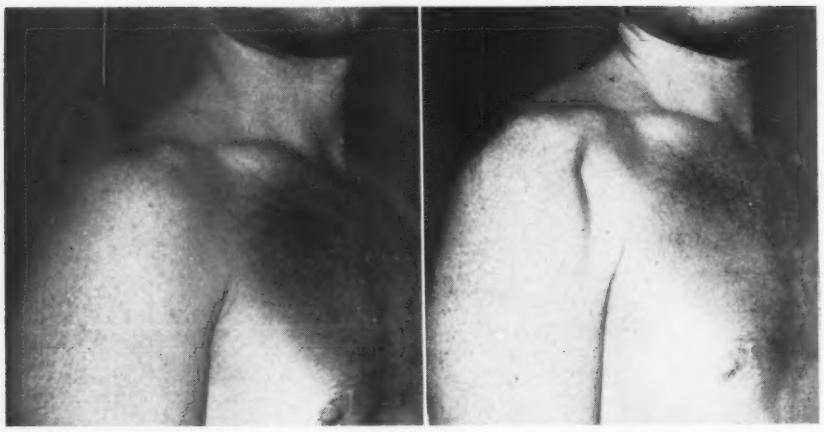
The patient was a twenty-two year old male medical student. Ever since he could remember he had been able to perform unusual movements with various joints, including both shoulders. These unusual movements of the shoulders, he was later informed, consisted of dislocating the head of the humerus posteriorly. Neither he nor his parents could recall any traumatic or other type of episode affecting the shoulders.

The patient had always performed the dislocation and reduction with great ease and without any pain. Both shoulders could be dislocated with equal facility, either together or separately. The dislocation did not occur involuntarily and the patient had at no time suffered any disability as a result of the condition of his shoulders; he had taken part freely in sports such as putting the shot, judo and swimming, and had completed his routine military training.

As far as the patient was aware, no members of his family possessed his specific ability in respect to either the shoulder joints or other joints.

The patient was well built and normally proportioned. Inspection of both shoulders with the patient at rest revealed no abnormalities. However, the shoulders possessed a greater range of active and passive movement than normal.

Dislocation of the right and/or left shoulder could be produced at will by muscular effort, easily and rapidly with the arm hanging by the side. The dislocation was accompanied by a clicking-crunching sound. The patient was able to maintain the dislocation with ease and with only slight muscular effort. Reduction was achieved by simply relaxing the shoulder musculature when the humeral head slipped back into position.



1A 1B

FIG. 1. Anterolateral view of right shoulder before dislocation (A) and when posteriorly dislocated (B). In the latter, note the triangular depression below the lateral end of the clavicle and the posterior bulge produced by the head of the humerus.

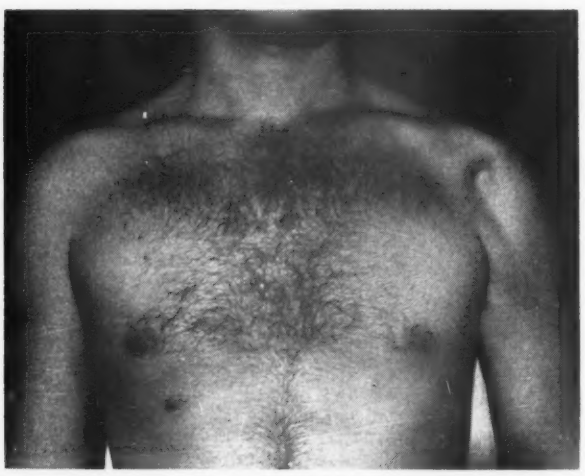


FIG. 2. Anterior aspect of right shoulder (undislocated) and left shoulder (dislocated). In the latter, note the triangular depression below the lateral end of the clavicle.

Inspection of the dislocated shoulder (right or left) showed slight flattening below the acromion. (Fig. 2.) Anteriorly the joint was flattened and presented, furthermore, a depression, triangular in shape approximately 1 inch wide at its base and 1½ inches long with the apex directed downward. (Figs. 1B and 2.) This depression was situated immediately below the lateral end of the clavicle, and through its floor the anterior margin of the glenoid cavity could be palpated. The coracoid process was prominent.

Posteriorly a bulge produced by the dislocated head of the humerus was clearly visible and palpable. (Fig. 1B.) On the right side it was located deep to the posterior part of the deltoid immediately inferior to the scapular spine where this became continuous with the acromion. On

FIG. 3. Anteroposterior roentgenogram of left shoulder taken during voluntarily produced posteroinferior dislocation. Note the distorted true joint space as a translucent triangle.

the left side the humeral head was not as prominent and not quite as high as on the right. The scapula itself, on both sides, projected posteriorly, being elevated from the thorax, and was rotated with the inferior angle approaching the vertebral column.

With the joint in a state of dislocation the patient was able to carry out considerable movement of the arm while maintaining the dislocation. For example, on the right the arm could be flexed to

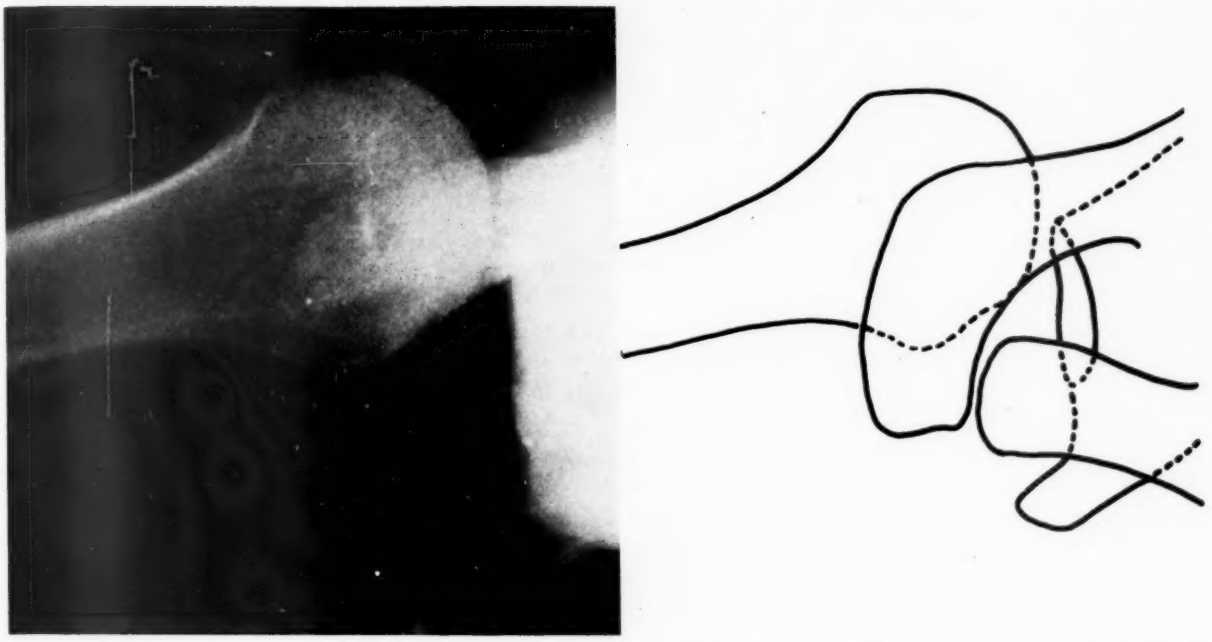


FIG. 4. Axial roentgenogram of right shoulder taken during voluntarily produced posterosuperior dislocation, together with explanatory outline drawing.

90 degrees in the sagittal plane and then, with accompanying rotation of the scapula, could be raised vertically above the head.

In addition to being able to dislocate the shoulder with the arm hanging by the side, the patient was able to do so with the arm held either vertically above the head (right side only), in 90 degrees or less of flexion (left side much more difficult than right), in 90 degrees or less of abduction (right side only) or adducted across the chest wall (right side only). Whenever dislocation could be achieved, reduction could also be carried out at will. In all instances the dislocation was posterior; neither with the arm hanging by the side nor in any of the alternative positions mentioned could the patient produce a dislocation in any other direction. Posterior dislocation could also be achieved passively by pressing firmly on the anterior aspect of the humeral head, provided that the muscles in the region of the shoulder joint were completely relaxed. Immediately after the pressure on the humeral head was released, the dislocation reduced itself spontaneously. Passive dislocation could not be produced if the patient resisted. Anterior dislocation could not be produced passively even with complete relaxation of the shoulder musculature.

Examination of the other joints of the body revealed hypermobility in the joints of the vertebral column, the elbow joints, the joints of the fingers and thumbs, and the hip joints. The latter could be actively abducted to 90 degrees and markedly hyperextended.

Physical examination showed also that over the dorsal aspect of the elbows folds of skin larger than normal could be drawn out. Elsewhere there was no evidence of excessive elasticity of the skin.

Roentgenograms of the shoulder joints taken while they were dislocated confirmed the clinical findings of a posterosuperior dislocation on the right side and a posteroinferior dislocation on the left. (Figs. 3 and 4.) The triangular area of increased translucency medial to the humeral head seen in the anteroposterior view of the dislocated left shoulder (Fig. 3) was probably due to the true articular space [*9,15*], distorted by the dislocation; a similar area of translucency was seen in the anteroposterior roentgenogram of the dislocated right shoulder. The true articular space was also seen in its normal crescentic shape in the neutral anteroposterior views of both shoulders.

The head of the humerus, both right and left, showed no defect or any other pathological changes, and the same applied to the glenoid fossa.

COMMENTS

The clinical and radiological findings indicate clearly that this is a case of purely voluntary dislocation of both shoulder joints.

The roentgenograms in our case bring out two points of interest. First, there was no tendency for the humeral head to be drawn into the infraspinous fossa (Fig. 4); in traumatic dislocation this tendency is often present, with resultant overlap of the glenoid and humeral head shadows in anteroposterior films

[*11,13,14*]. In our case the anteroposterior film showed a gap between the glenoid and the humeral head. (Fig. 3.)

Second, the true articular space [*9,14*] was clearly seen when the joints were voluntarily dislocated. (Fig. 3.) This space can often be demonstrated in infants and children in the normal shoulder joint as well as in other joints, and sometimes in the shoulder joint of adults. As far as we are aware, the true joint space has not been demonstrated previously in a case of posterior dislocation of the shoulder joint.

According to Reischauer [*6*] the phenomenon of purely voluntary dislocation of the shoulder joint is dependent on two factors. In the first place the patient must possess the ability to contract the muscles which produce the dislocation without simultaneously contracting their antagonists. This signifies a special type of neuromuscular coordination, which, in the opinion of some authors [*3,6*], can be learned; Tommasini [*12*] speaks of an acquired faculty of "dissociating" the actions of various muscles. Fried [*2*] has also discussed this mechanism.

In the second place an increased elasticity of the joint capsule and its ligaments must exist. This is not simply a laxity; the latter would make for instability of the joint, whereas in cases of purely voluntary dislocation the joint is completely stable. As evidence of the greater elasticity of the capsule in our case may be cited the fact that the humeral head immediately returned to its original position without muscular action after being passively dislocated.

Further evidence of increased elasticity is the greater range of movement, without instability, seen in joints other than the shoulder joint. This feature and the increased elasticity of the skin in the elbow region in our case raise the possibility of there being some connection between cases of purely voluntary dislocation and the syndrome of Ehlers-Danlos [*4,5*] (hyperelasticity of the skin with hypermobility of the joints). Riedinger [*7*] also remarked on the increased elasticity of the skin in this case of voluntary dislocation of the shoulder joint.

Another point of interest is that the dislocation in our case was posterior, as in almost all previously reported cases of purely voluntary dislocation of the shoulder joint. Acute traumatic dislocations, as well as habitual and habitual-voluntary dislocations, are seldom posterior. Why the dislocation in purely voluntary cases is predominantly posterior is problematic; it may be that in a capsule which has not been subjected to trauma the site of least resistance is posterior, where no glenohumeral thickening exists.

With regard to prognosis and treatment, the opinion of some workers [*6*] is that there is no indication for any treatment, as no complications are likely to arise. However, in each of Tommasini's [*12*] three cases pain developed in the joint after some time, and in one of these cases an erosion of the cartilage of the humeral head was found at operation. It would therefore seem advisable to persuade persons capable of voluntarily dislocating their joints to do so as infrequently as possible.

SUMMARY

A case of purely voluntary bilateral posterior dislocation of the shoulder joint is described. There was no history of trauma and no evidence of joint disease.

The possible factors underlying the capacity to dislocate the shoulder joint voluntarily are briefly discussed.

The true articular space, in a distorted form, was demonstrated in the roentgenograms of the dislocated joints.

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Since 1900:

1900 Wertheim introduces operation for uterine cancer
1901 Takamine isolates epinephrine
1902 Carrel introduces methods of vascular anastomosis and transplantation of tissue
1903 Bruce shows that sleeping sickness is transmitted by the tsetse fly
1904 Atwater invents respiration calorimeter
1905 Schaudinn discovers parasite of syphilis

Rupture of the Thoracoacromial Artery in Anterior Dislocation of the Shoulder

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VASCULAR complications following dislocation of the shoulder are rather infrequent in our present type of civilization. Cranley and Krause [*1*], who reviewed the literature from 1918 to 1956, could find only eight such cases to report and added two cases of their own. Two new cases of damage to the axillary artery have been reported by McKenzie and Sinclair [*2*]. However, prior to 1911 Guibé [*3*] succeeded in reporting fifty-seven cases collected from ten different authors. It appears that this type of complication was more frequent in the horse and buggy days. Indeed, Guibé states that one of the prevalent mechanisms that occurred in this type of injury was for a horse to rear up suddenly and pull on the driver's extended shoulder; another mechanism came into play when a person fell out of a buggy and was dragged by an extended arm. Today the most common cause of dislocation of the shoulder is a fall on the extended arm, as illustrated in the following case:

The patient, a forty-seven year old schoolteacher, was seen in the clinic with a history of falling down basement stairs and dislocating her left shoulder. At the time of admission she complained of severe pain in the left shoulder, and x-ray examination confirmed the diagnosis of anterior dislocation. Her past history was not relevant except for a history of a shoulder dislocation six years prior to this accident. Reduction was attempted with the patient under Vinethene® anesthesia, using the Kocher maneuver. When this failed the reduction was finally accomplished, with difficulty, by the Cooper (Hippocrates') method. Immediately following reduction a bluish discoloration appeared along the anterior axillary fold. Examination revealed no loss of sensation and a radial pulse of good volume. Because the patient was experiencing severe pain and also because of the unusual findings of ecchymosis and tension in the axillary area she was admitted to Nankin Hospital. At 7:00 P.M. (six hours after admission) the patient showed progressive symptoms of shock for which she received a blood transfusion. Following the transfusion the patient rallied for a short time, but symptoms of shock reappeared with concomitant evidence of spreading of the ecchymosis and increase of tension in that area. All these findings prompted the decision for surgical intervention. With the patient under Surital® anesthesia, a U-shaped incision was made over the upper portion of the pectoral and brachial areas. The incision was carried down to pectoralis major fascia and muscle. The pectoralis muscle was detached as is done in radical mastectomy, and the insertion of the pectoralis minor was cut transversely. The clavipectoral fascia was incised and the blood clots were evacuated. Removal of the deeper part of the clot brought a jet of bright red blood hissing from the depth of the axilla; this was controlled by finger pressure on the axillary artery, and repair of the vessel was done with interrupted No. 5-0 silk sutures. The wound was closed in layers and one drain was placed into the depth of the axilla. The patient was returned to her room in good condition and recovery progressed satisfactorily.

Guibé [*3*] makes several pertinent comments as to locations of the laceration and mechanisms by which these accidents occur. He states that the most commonly torn collaterals are, respectively: subscapular, circumflex and, more rarely, the long thoracic arteries. In the case reported herein the thoracoacromial trunk was torn from the axillary artery. Guibé also noted that the Cooper type of reduction is more prone to cause blood vessel damage than the Kocher. It is trite to say that violence is a *sine qua non* of shoulder dislocation and that the intensity of the violence could be sufficient to cause the head of the humerus to damage the axillary artery or one of its collaterals.

Guibé [3] explains the delayed appearance of ecchymosis in the axilla, in a number of cases in which the Cooper method was not used, by the tamponade action of the head of the humerus against the axillary artery. Reduction of the dislocation permits active hemorrhage from the axillary artery to take place. It is not to be denied that violence to the axillary artery could also be the result of a misguided attempt to reduce the dislocation of the shoulder.

ANATOMICAL CONSIDERATION

In order to explain why the acromioclavicular artery was severed, it is necessary to review the anatomy of the clavipectoral fascia. In addition to helping form the anterior axillary wall, this fascia attaches laterally to the coracoid process and medially to the first costal cartilage. Inferiorly it envelops the pectoralis minor, while superiorly it envelops the subclavius muscle and becomes continuous with the periosteum of the clavicle. The acromioclavicular artery usually arises from the second part of the axillary artery, curves around the medial or superior border of the pectoralis minor muscle, and, upon piercing the clavipectoral fascia, immediately divides into its branches. The clavipectoral fascia, particularly if well developed, encloses the root of the acromioclavicular artery and thus any extreme stretching or pulling of the fascia might conceivably sever the artery at its origin. (Fig. 1.) Severing of the acromioclavicular artery is also observed routinely in the dissecting laboratory when attempts are made to clean its branches. The only other eventuality by which the artery could be torn might occur during the reduction of a humeral dislocation. Any excessive stretching of the axillary artery might conceivably pull the acromioclavicular artery away from the clavipectoral fascia; however, this accident is unlikely since the subscapular or posterior circumflex humeral arteries would most likely be torn first [1] and there is no evidence of this having occurred. Thus, it is clear that the acromioclavicular artery was torn or severed during the dislocation.

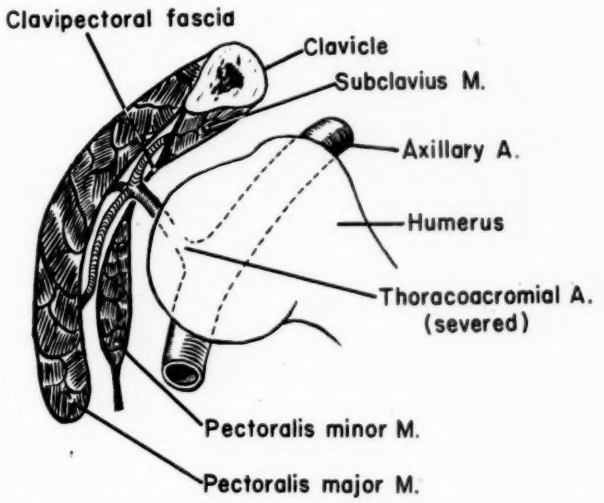

FIG. 1. This drawing shows how the dislocated head of the humerus displaces the axillary artery thereby tearing the acromioclavicular artery at its origin. The anchoring effect of the clavipectoral fascia on the acromioclavicular artery facilitates such a process.

SUMMARY

It may be said that vascular complication following shoulder dislocations still happens and should bring prompt surgical intervention. The Kocher method is the procedure of choice, reserving the Cooper method as a last resort.

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Argentaffine Tumour of the Jejunum with Perforation

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In 1953 Willis [*12*] stated that the argentaffine carcinomas of the small intestine were still insufficiently known to pathologists and surgeons. This is hardly surprising as the condition is so rare that the individual worker is unlikely to meet with more than half a dozen cases during his lifetime. In 1933 Raiford [*8*] could find only nine examples among 62,000 pathological specimens at the Johns Hopkins Hospital, while in 1943 Dockerty and Asburn [*6*] found thirty instances in the histological material accumulated at the Mayo Clinic between 1906 and 1943. In 1939 Ariel [*1*], in his review of the literature, stated that 237 cases had been published and in 1942 Dangremond [*5*] added forty-six to these.

The gross features of the tumour are as follows: At least half the patients have multiple growths and these may be distributed through both ileum and jejunum. Spread of the growth is along the mucosa and submucosa rather than outward to the peritoneum or inward as a polyp. This feature, producing local rigidity, prevents infolding of the gut wall. Intussusception is thus a rare manifestation and has only been recorded three times. In Ariel's series there was one in a man fifty-two years old and one in a man thirty-two years of age, while in 1958 McCartney and Stewart [*10*] described one in a boy of ten.

This superficial spread of the tumour tissue also makes perforation unlikely. In the unusual event of the tumour spreading widely under the serous coat wide areas of this aspect show smooth white zones and it is in these areas that perforation occurs, probably as a sequel to an interruption of the blood supply. Metastasis to the mesenteric lymph glands and to the liver is a frequent complication and both the primary growths and the metastases may show the remarkable attribute of achieving a large size and then remaining stationary for long periods. In 1930 Cope [*4*] described how a short circuit operation was carried out to relieve a partial obstruction and eight years later the patient, although still having large palpable masses, appeared in excellent health.

Microscopically the tumours are composed of rounded solid masses of polyhedral cells separated by zones of fibrous reaction. These may merge to form large cell masses which advance to obliterate the mucosal epithelium and produce ulceration. The tumour cells, like the Kulchitsky cells of the crypts of Lieberkühn, show granules with an affinity for silver salts and are accepted as being derived from them. Occasionally the tumour tissue shows small glandular acini which may give the false impression that the structure is an adenocarcinoma.

The age at which the tumour comes to light is usually between fifty and seventy. In Ariel's series the age was ascertained for seventy of the patients and the mean age was *57.5*. The average age of the six patients who came to necropsy as recorded by Willis [*11*] in 1940 was sixty years. However, as at least half of the recorded cases were unexpected discoveries at autopsy the age at which symptoms develop must be a good deal less. The second most frequent manifestation is the development of intestinal obstruction. Among the seventy-nine cases said by Ariel to have occurred between 1930 and 1938, no less than thirty-three were of this type.

Less than a tenth of the cases arise in one of the following ways: perforation and an acute emergency, intussusception, the discovery of a painless abdominal mass, or

the "Flushing syndrome" described in 1952 by Biörck et al. [2] and caused by the secretion of 5-hydroxytryptamine.

CASE REPORT

A fifty-nine year old woman was admitted to the hospital with a history of mild indigestion, insufficient to make her seek medical advice, for two years. Six hours before admission severe epigastric and left sided abdominal pain developed. She vomited several times and passed three stools of normal appearance. On examination all areas of the abdomen were tender and tympanitic. There was no muscle rigidity but pronounced guarding was present. There was marked tenderness on rectal examination and a hard mass was felt in the rectovaginal pouch. A provisional diagnosis of perforation of a peptic ulcer was made.

At operation the abdomen was opened through a left paramedian incision and a small amount of purulent fluid was found in the left side of the peritoneal sac. This was found to be issuing from a tiny perforation in a hard craggy tumour mass lying 15 cm. below the duodenojejunal junction. The adjacent mesentery was massively thickened and there were several firm glands, each less than 1 cm. in diameter, in the root of the mesentery. The growth was resected and an end-to-end anastomosis carried out. The cluster of glands was removed. Recovery from the operation was uneventful. Examination of the urine during convalescence showed no excess of 5-hydroxy-indole-acetic acid. The value of this test in disproving the presence of other tumour masses is, according to Macfarlane [7] not yet proved.

On pathologic examination the preserved specimen of gut was 18 cm. long. (Fig. 1.) Extending to within 3 cm. of one end was an ulcerated growth occupying 10 cm. of the long axis of the gut. The gut wall was up to 1.5 cm. thick and there was a massive hard white extension into the mesentery. The outer aspect of the tumour showed large smooth white areas beneath the peritoneum and in the centre of one of these, on the free border of the gut, was a perforation 2 mm. in diameter.

Sections showed that the tumour was composed of compact masses of polyhedral cells embedded in fibrous stroma. In some areas large cell masses replaced the mucosa and in others spread widely under the peritoneal coat. No tumour deposits were found in the cluster of glands removed. Sections stained by Levaditi's method showed an abundance of the characteristic silver staining granules in the cytoplasm of the tumour cells. No cells of this type were found in the lymph glands.

COMMENTS

This case is, we believe, the third recorded occurrence of perforation in an argentaffine tumour of the small intestine. In 1931 Cooke [3], among his eleven cases, describes a man of sixty who had been under observation for recurrent epigastric pain. During an especially intense bout laparotomy was performed. An ileal tumour 4.5 cm. in diameter was found to have perforated; there was free yellow fluid in the peritoneal cavity and the liver was studded with metastases. The patient died fourteen days after the operation.

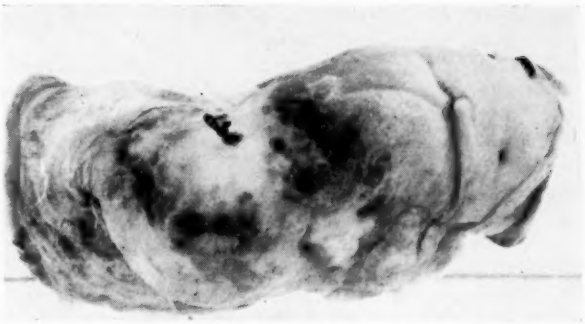

FIG. 1. A marker has been placed in the perforation which is situated in the centre of a white tumour mass.

In 1951 Stewart and Thomson [10] describe the same accident in an Iranian woman aged forty. At the time of the annual religious fast she drank a large quantity of iced water and was seized with violent abdominal pains which passed off after a few hours. Similar attacks then recurred every two or three weeks for a year and she was admitted to the hospital during a bout. Her abdomen was swollen, tender and silent and a hard mass was felt above the right fornix during vaginal examination. Three large tumours were found in the ileum at operation and there was a perforation in the lowest of the three. No sign of metastases was found. The tumours were excised and anastomoses carried out. She recovered rapidly and insisted on leaving the hospital on the eleventh day after operation.

The case herein recorded and the two previously reported may, it is hoped, form a nucleus for the accumulation of information about this very rare accident.

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In October 1958 the United States Department of Commerce, Bureau of the Census, reported the population of the United States was about 175,000,000 people. One birth occurred every seven and a half seconds, one death every twenty seconds, one immigrant arrived every one and a half minutes and one emigrant left every twenty minutes. The net gain in population was one in every eleven seconds.

Intestinal Obstruction

A COMPLICATION OF ANTICOAGULANT THERAPY

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SINCE the first clinical trials of heparin in 1937, and dicumarol in 1941, there have been many reports in the literature of untoward effects in the form of hemorrhage [*1*]. Although hemorrhage is the only known complication to anticoagulant therapy, there are many contraindications. Poorly controlled hemostasis in large open areas following surgery, brain and spinal cord surgery, blood dyscrasias with hemorrhagic tendencies, malignant hypertension, and subacute bacterial endocarditis are the more important contraindications. However, the most important contraindication is that of inadequate laboratory facilities especially when combined with inexperience in the use of these drugs.

In a review of the literature, Rainie [*2*] cites the reports from Mayo Clinic in 1947 and 1948, indicating an incidence of minor bleeding in about 4 per cent and serious bleeding in about 2 per cent of patients receiving anticoagulants. Of fifty patients with myocardial infarction treated with heparin and dicumarol, only one case of untoward bleeding (uncomplicated hemarthrosis) occurred.

Wright and Rothman [*3*] emphasize the lack of correlation between the prothrombin percentage and the bleeding tendency in a report on four patients with dicumarol poisoning. Of their patients, two died from gastrointestinal hemorrhage, one from cerebral hemorrhage, and one from pulmonary hemorrhage; in each case the prothrombin percentage was within the accepted therapeutic range.

Fatal retroperitoneal hemorrhage caused by lumbar sympathetic block used in conjunction with controlled anticoagulant therapy has been stressed in several reports [*4,5*]. Since O'Connor et al. [*6*], demonstrated fatal bleeding even while the induced hypoprothrombinemia was within therapeutic range, they are of the opinion that all deep needle-puncture procedures are contraindicated during dicumarol therapy and that they had best be carried out three or four hours after the last previous dose of intermittent heparin therapy.

Berman and Mainella [*7*] reported two cases in which there was hemorrhage into the intestine requiring resection in patients on anticoagulants following myocardial infarctions.

With this brief review in mind, the following case is presented.

CASE REPORT

L. A., a seventy-two year old Negro woman, was admitted to the John Gaston Hospital, Memphis, Tennessee, on October 11, 1957, with a history of cramping lower abdominal pain of four days' duration. The patient had vomited bile-stained material on six to eight occasions two days prior to admission. On the morning of October 11, she fainted while getting out of bed but regained consciousness in a few minutes. There was no history of intolerance to food, hematemesis, melena or diarrhea. There were no symptoms referable to the cardiorespiratory system. The patient had noted no bowel movements for forty-eight hours prior to admission. No members of her family had noted any recent illness. Past history revealed that the patient was known to have had hypertension for fifteen years and had suffered a "slight cerebrovascular accident" in November 1956. Following this incident she was treated as an out-patient with dicumarol, digitalis and Raudixin.® Her prothrombin time had been maintained within therapeutic range up until the last clinic visit on September 27, 1957. Physical examination revealed blood pressure of 110/60 mm. Hg, atrial fibrillation with an apical rate of 120 per minute, and moderate abdominal distention with slight generalized tenderness. Laboratory studies showed a white blood cell count of 14,600 per cu. mm., hemoglobin 9.5 gm. per cent, CO_2 21 mEq./L., chlorides 92 mEq./L., sodium 134 mEq./L., non-protein

nitrogen 57 mg. per cent, and prothrombin time greater than 200 seconds. The results of urinalysis was normal and a flat plate of the abdomen revealed a distended loop of small bowel interpreted as jejunum. Wangensteen suction was begun, dehydration and blood volume deficit were corrected with intravenously administered electrolyte solutions and whole blood transfusions. Vitamin K_1 oxide and whole blood transfusions were used to correct the hypoprothrombinemia, and digitalis therapy was continued. The preoperative diagnosis was intestinal obstruction, secondary to hemorrhage into the bowel wall as a complication of dicumarol therapy. At operation there was 200 cc. of dark-colored blood present in the peritoneal cavity. A small hematoma was noted on the lateral wall of the first portion of the duodenum. Several small subserosal hemorrhages were noted scattered throughout the mesenteric border of the distal ileum. A large subserosal hematoma involving 10 to 12 cm. of jejunum was located 30 cm. from the ligament of Treitz. This segment of bowel was markedly distended and twisted upon itself 180 degrees with collapse of the intestine distal to this point of obstruction. Upon reduction of the volvulus and application of warm saline packs, the involved segment was found to be viable. The postoperative course was uneventful and the patient was discharged on the ninth postoperative day. She has been followed up closely in the out-patient department and dicumarol therapy has been reinstituted without further hemorrhagic episodes.

SUMMARY

A brief review of the complications of anticoagulant therapy is presented.

A case of intestinal obstruction secondary to dicumarol therapy is reported to illustrate the potential hazards of anticoagulants. It is emphasized that in order to administer these drugs with a reasonable degree of safety, a reliable laboratory and very close medical supervision of the patient are imperative.

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Pancreatic Apoplexy

REPORT OF A CASE TREATED BY PARTIAL PANCREATECTOMY, WITH RECOVERY

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THE case to be reported was unique in our experience, and a search of the recent literature has failed to disclose further instances. In view of the extremely high mortality of the disease, the unusual type of surgical treatment, and the patient's rather unexpected complete recovery, it is presented in detail herein.

CASE REPORT

This was the first admission to the Bellevue Hospital for A. L. (No. 31297-56), a thirty-five year old Negro man, on August 22, 1957, with a chief complaint of severe abdominal pain for twenty-three hours.

This illness had started three days prior to admission with mild epigastric discomfort. The patient stated that he had consumed a moderate amount of whiskey prior to the onset. On account of the persistence of the discomfort he had taken a larger amount than usual on the day before admission. Following this there was a sudden onset of sharp severe pain in the epigastrium and left upper quadrant, followed by repeated attacks of vomiting. The pain was dull, fluctuated in intensity, and eventually radiated to the right upper quadrant and to the back. The vomitus was liquid and yellow in color. His last bowel movement had occurred two days prior to admission. Physical examination revealed a well developed, well nourished Negro man weighing approximately 230 pounds.

His temperature was 101.4°F., pulse 110, respiration 24, blood pressure 190/120 mm. Hg. He was alert and cooperative but complained of persistent abdominal pain, constantly moving about restlessly in bed. The abdomen was tender and rigid all over and exquisite in the left upper quadrant. Rebound tenderness could not be definitely demonstrated. There was no palpable mass, and bowel sounds were present but sluggish. Rectal examination was non-contributory.

The results of laboratory studies were as follows: urinalysis—specific gravity 1032, albumin 0, sugar 4 plus, sediment negative; blood counts—hemoglobin 14 gm. per cent, white blood cells 12, 950 per cu. mm.; differential white cell counts, polymorphonuclear leukocytes 80 per cent, lymphocytes 14 per cent, basophils 6 per cent; amylase 390 rising to 690 units per cent (normal value 0–450 units), alkaline phosphatase 5.5 Bodansky units per cent, bilirubin 2.7 mg. per cent.

Gastric aspiration yielded clear gastric juice, guaiac negative with no free acid. An abdominal tap through a No. 13 trocar in the right lower quadrant yielded thick yellowish material, later found to have 2,400 units of amylase per cc. Chest and flat abdominal roentgenogram failed to show free air but were otherwise non-contributory. Hydration was instituted with intravenously administered fluids and electrolytes, and the patient was taken to the operating room about twelve hours after admission. Under general anesthesia exploratory laparotomy was performed. A small amount of cloudy fluid was present in the peritoneal cavity and, on palpation, a mass was detected posterior and inferior to the spleen. The lesser peritoneal cavity was entered through the gastrocolic ligament and approximately 200 cc. of cloudy fluid with fibrinous flakes was evacuated. The mass was found to be an acutely inflamed pancreas with the inflammation limited to the tail and part of the body. The involved pancreas was resected at the body (approximately 40 per cent of the gland), together with two small accessory spleens. Hemostasis was secured with ligatures and sutures.

Postoperatively the patient was treated with continuously intravenously administered fluid, Levin tube drainage from the stomach, and sump drainage of the lesser peritoneal cavity. Seven thousand

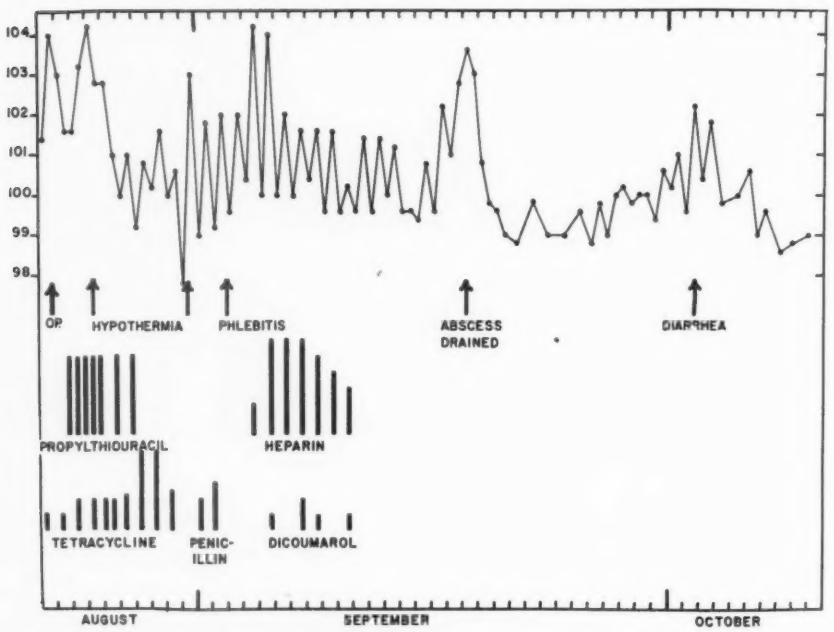

FIG. 1. Clinical course of patient. Maximal daily dosage of drugs administered are as follows: propylthiouracil, 3,000 mg.; heparin, 240 mg.; tetracycline, 1,000 mg.; penicillin, 1.8 million units; dicoumarol, 400 mg.

milligrams of propylthiouracil was given in divided doses over a five-day period via the Levin tube. An ice water mattress was used to control hyperpyrexia. The patient's course was further complicated by the development of hallucinations, thrombophlebitis, wound sepsis and gangrene of both heels, but these responded well to standard therapeutic measures. The postoperative course is summarized for the sake of brevity in Figure 1. The patient was last seen April 17, 1958 at follow-up clinic. He had no subjective complaints and weighed 255 pounds. He ate all foods and stated he drank "a little now and then." The wound was well healed and no masses were palpable. A gallbladder series on February 25, 1958 visualized the gallbladder with good concentration after a fatty meal. The area of the resected pancreas showed diffuse calcification. The results of a secretin test made on December 19, 1957 showed marked pancreatic dysfunction consistent with a diagnosis of chronic pancreatitis. Volume was 153 cc. (normal 90–260 cc.), bicarbonate 138.7 mEq./L. (normal 90–120 mEq./L.), amylase 20.4 units per cent (normal 275–1,100 units).

There was no diabetic curve after a four-hour glucose tolerance test. Further secretin studies will be performed in the future to evaluate the course of pancreatic function.

The pathologic report was as follows: The specimen consisted of a 7 by 6 by 5 cm. portion of red-brown pancreatic tissue. On sectioning, the pancreatic architecture was obscured by large, soft hemorrhagic areas and zones of edema. Microscopic sections showed a necrotizing process involving the parenchyma and interstitial connective tissue. The pancreatic lobules showed necrosis, hemorrhage, and acute inflammatory infiltration. The edematous interstitial connective tissue was filled with hemorrhage and acute inflammatory cells. Zones of fat necrosis were present. (Figs. 2 and 3.)

COMMENTS

In 1874, Zenker [1] described a type of catastrophic hemorrhagic necrosis of the pancreas as "pancreatic apoplexy." In 1910 Hofmann [2] cited a similar case for which he had operated; only drainage was performed, and the patient died. In his discussion of the problem, he made the following observation: "Finally I should like to make a proposal as to treatment: I consider drainage . . . as needless. At autopsy in the case cited, the thrombosed portion of the organ . . . shelled out so easily that . . . I am perfectly convinced that it would have been just as easy and bloodless in the living patient . . . In the next case, provided it appears technically easy, I would do it with a calm conscience." Certainly, under the circumstances in our case, his suggestion appears to have been a good one, although at the time none of us was aware of his writing. The removal of this necrotic and potentially dangerous tissue might be expected to have, and indeed did have, a

FIG. 2. Pathologic specimen, low power view. Note spotty lobular necrosis and interstitial edema. The major duct is not dilated. Hemorrhagic fat necrosis is prominent.

FIG. 3. Pathologic specimen, higher power view. Note fat necrosis, inflammatory and hemorrhagic exudate, and diffuse necrosis of lobular parenchyma in this area.

favorable influence on the progress of the disease. Technically it presented no great difficulty, and there was little or no necessity for blood vessel ligation. It is interesting that Hannon and Sprafka [3] have recently advocated resection in traumatic pancreatitis, and reported three cases in which this was successfully performed. A point of further interest is that this case has provided us with the pathologic picture, gross and microscopic, of hemorrhagic pancreatic necrosis in a stage of development rarely if ever observed by the pathologist. By the time death ensues, the autolytic process has largely destroyed any evidence as to the origin of the catastrophe. In the present case, it is most interesting to note the points of simi-

larity between the human disease and that experimentally produced by us in animals [4]. On the basis of the latter experiments and others to be reported we have come to realize the importance of vascular insufficiency in the etiology of acute hemorrhagic pancreatitis. The pathologic picture presented by this patient (relatively undisturbed as it is by autodigestive processes), supports, we believe, the contention that the human disease as well owes much if not all of its origin to vascular insufficiency.

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People are far more health-conscious than they used to be. Thirty years ago, for example, a much lower proportion of the population consulted a doctor during a given year, and the average number of visits per person was only half what it is today.

Moreover, the use of physician visits for health examinations, immunizations and other preventive services has increased. Not so long ago consulting a doctor was often considered a sign of weakness; now it is recognized as common sense in times of health as well as sickness.

Volvulus of the Right Colon Complicating Subhepatic Cecum

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Subhepatic cecum is not rare. The ordinary pattern, resulting from complete non-descent, has been described as follows [*1*]:

"Generally speaking, the cecum and base of the appendix are incorporated within and behind the anterior fold of visceral peritoneum, pointing upward and/or medially toward the gallbladder and pylorus. The right colon drops for a short distance as a festoon, redoubling upon itself to join the hepatic flexure. There is no shortening of the ascending colon. The terminal ileum loses its mesentery near the normal site of the ileocecal junction and extends upward in a retroperitoneal position to meet the high cecum, entering from behind and medially. The blood supply of the cecum and appendix also follows the ileum upward retroperitoneally." (Fig. 1.)

High fixation of the cecum, with an entirely free, looped right colon hanging as a festoon, together with firm fixation at the hepatic flexure, strongly predisposes to a volvulus [*2–5*] of a type strikingly different from that usually encountered and often described as occurring in a mobile cecum [*6–14*].

CASE REPORT

A sixty-six year old man was hospitalized because of aching pain in the right upper quadrant of the abdomen and right shoulder, which had started four days previously. His abdomen had become distended, so he had taken enemas, with satisfactory results the first and second days. Because of discomfort he had taken little nourishment.

Examination revealed a thin, elderly man with an unduly prominent, diffusely tender, tympanitic and silent right hypochondrium. The blood pressure was 136/72 mm. Hg, pulse 78, and respirations 14 per minute.

Roentgenograms disclosed an enormously distended bowel filling the right abdomen, elevating the diaphragm and replacing the liver shadow. (Fig. 2.) The white blood cell count was 13,900 per cu. mm., with a differential of 78 per cent neutrophils and 22 per cent lymphocytes. The red blood cell count, hemoglobin and urinalysis were within normal limits.

Surgical exploration of the abdomen made evident the presence of a tremendously distended loop of bowel which occupied the right anterior subphrenic space, completely displacing the liver downward and to the left. This was identified as colon involved in a closed loop obstruction due to a volvulus at the firmly fixed hepatic flexure. (Fig. 3.) There was complete non-descent of the cecum, which was attached high in the subhepatic position by a dense peritoneal fold and an immobile retroperitoneal segment of ileum. The completely free, looped right colon, held firmly at each end, had by progressive distention become directed upward to occupy the entire anterior subphrenic space.

Extreme distention first necessitated partial decompression by aspiration through a large needle. This allowed delivery of the closed loop from its subphrenic site and detorsion upon return to its accustomed position. The appendix, inflamed and later described as "strangulated," was dissected free and removed. (Fig. 4.) The damaged but viable cecum was then mobilized by division of its peritoneal attachment and exteriorized through a small incision in the right mid-abdomen, providing both an excellent cecostomy and a preventive measure against later recurrence of the volvulus.

The patient's condition during and immediately following operation was satisfactory, except for cyanosis which was relieved by bronchial aspiration. He rapidly gained strength on supportive therapy and the cecostomy functioned satisfactorily when opened the following day. Peristalsis returned, so feeding was resumed without difficulty. He was soon up and about without complaint.

FIG. 1. Barium study of subhepatic cecum. The free, looped right colon hangs as a festoon from the firmly fixed high cecum and closely approximated hepatic flexure.

FIG. 2. Roentgenogram showing volvulus of the right colon complicating subhepatic cecum. The free, looped right colon, held firmly by high fixation at each end, has by progressive distention become directed upward to occupy the anterior subphrenic space.

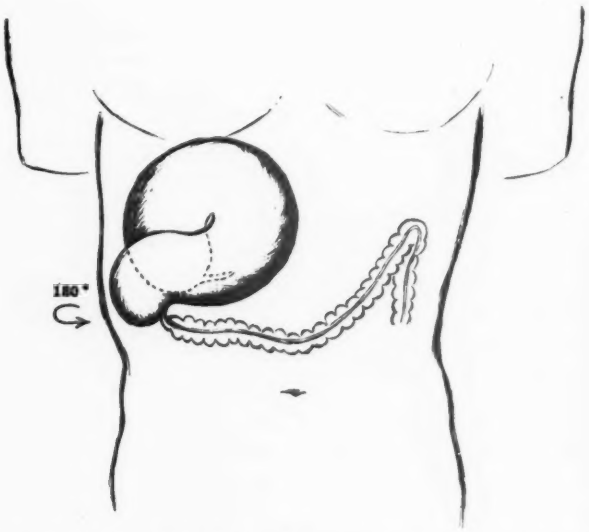

FIG. 3. Volvulus of the right colon complicating subhepatic cecum. Closed loop obstruction has resulted from an anterior and left 180 degree twist at the hepatic flexure. The extremely distended, subphrenic right colon has become coiled upon itself because of fixation of the cecum. The liver has become displaced downward and to the left.

FIG. 4. Subhepatic cecum after partial decompression and detorsion. The appendix, pointing upward and left, has been freed from its peritoneal attachment. The cecum is held firmly in upright position by a peritoneal fold.

Late in the afternoon of an excellent eleventh postoperative day, severe generalized abdominal pain developed suddenly, followed by vomiting, circulatory collapse and loss of consciousness. Efforts to combat profound shock were unsuccesful and the patient died early the following morning.

The cause of death was shock due to a sharply demarcated segment of gangrene of the ileum lying between two points, located 100 and 25 cm. proximal to the ileocecal valve.

The final diagnoses were: (1) volvulus of the right colon complicating subhepatic cecum; (2) mesenteric infarction occurring on the eleventh postoperative day.

COMMENT

Attention is again directed to subhepatic cecum as a source of serious and confusing abdominal disease.

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Spontaneous Perforations of Combined Benign Ulcers, Gastric and Duodenal

A. H. Haseeb, M.B., CH.B., *London, England*

Only five cases of double perforations of peptic ulcers have been reported in the literature. As the incidence of combined ulcers is 10 to 25 per cent (Maingot [1]), it is likely that the incidence of simultaneous perforations is higher than is realised. Therefore, the following case is presented of a patient with free preforation of both a gastric and a duodenal ulcer.

CASE REPORT

The patient, a seventy-nine year old man, had had a history of duodenal ulcer since 1950. He was admitted to the hospital on November 28, 1957 at 9:30 P.M., with an acute condition of the abdomen and severe abdominal pain. Two hours before admission to the hospital, he was seized with severe upper abdominal pain as he was getting out of bed. Pain doubled him up and he felt very "sore" afterwards. Apparently, the day before admission he had had an attack of abdominal pain but of a less severe nature. Prior to admission, he vomited blood stained material and passed melaena stools. Shortly after admission to the hospital, he had severe haematemesis.

On examination, the patient was in a severe state of shock. Temperature was 97°F., pulse 110, and blood pressure 155/100 mm. Hg. There was no cyanosis, the tongue was dry and furred, and the patient was lying still in bed. The abdomen showed no movement; there was generalised tenderness and board-like rigidity. Liver dullness was diminished. Bowel sounds were absent. Proctologic examination showed traces of blood on examining finger. The case was diagnosed as a perforated peptic ulcer. I decided to operate immediately; a transnasal Ryle tube was put into the stomach, and intravenously administered 0.18 per cent saline infusion was started.

The general anaesthesia was administered at 11 P.M. A high right paramedian incision was used to open the abdomen. A profuse amount of purulent fluid, chocolate-coloured, was present in the abdominal cavity. The fluid was sucked out and the stomach exposed. A large prepyloric perforated ulcer about .75 cm. in diameter was seen on the lesser curvature. I had a little difficulty in suturing the ulcer as the surrounding tissues were oedematous and friable, and I had to take the needle-bites a little farther away from the ulcer margin. It was closed and covered with a patch of omentum. During the process of "mopping up," I examined the duodenum before closing the abdomen, and much to my surprise I found a large perforated duodenal ulcer, about .5 cm. in diameter and 2 inches distal to the gastric ulcer just sutured. I had no difficulty in suturing this second ulcer, and covered its site with a patch of omentum. Mopping up was completed and the abdomen was closed without drainage.

The patient's postoperative progress was as follows: Intravenously administered glucose-saline solution, 0.18 per cent, was continued at the rate of 2,000 ml. per twenty-four hours during the first two postoperative days (intravenously administered Aureomycin,® 500 mgm. was added to each litre bottle of the saline drip and maintained for five days). The saline drip was increased to 3,000 ml. per day after the first forty-eight postoperative hours. Paralytic illeus with abdominal distention was still very marked until the fourth postoperative day when the blood electrolyte showed: sodium 141 mEq., chloride 95 mEq., and potassium 2.5 mEq. As the potassium was very low, 100 mEq. was given intravenously (as potassium chloride, 50 mEq., to a litre bottle of the saline drip). On the fifth postoperative day the abdominal distention was definitely less marked and a few bowel sounds were heard. Hematologic potassium was 3 mEq. A further 50 mEq. of potassium chloride was given through the drip. In the evening of the fifth day, the patient passed flatus which was followed by bowel motion. The drip and the Ryle tube were taken down. The patient was next started on fluids taken by mouth, followed by a light gastric diet. His general condition continued to progress satisfactorily until the twelfth postoperative day when the patient started to be subject to occasional vomiting, mainly after meals, and sug-

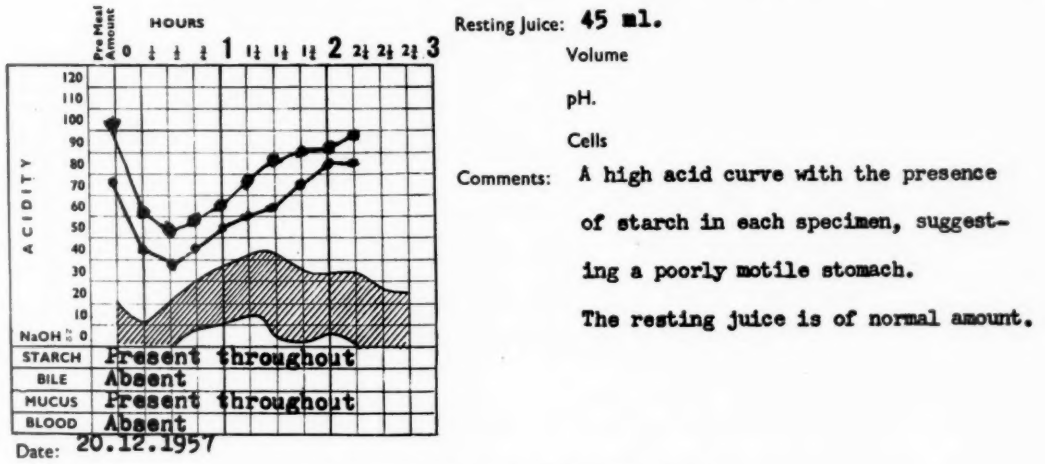
Pre Meal Amount
HOURS
0 ½ ½ ¾ 1 1¼ 1½ 1¾ 2 2¼ 2½ 2¾ 3
ACIDITY
120 110 100 90 80 70 60 50 40 30 20 10
NaOH N/20 0
STARCH Present throughout
BILE Absent
MUCUS Present throughout
BLOOD Absent
Date: 20.12.1957
Resting Juice: 45 ml.
Volume
pH.
Cells
Comments: A high acid curve with the presence of starch in each specimen, suggesting a poorly motile stomach.
The resting juice is of normal amount.

FIG. 1. Results of fractional test meal.

gested to be due to pyloric stenosis. This was confirmed by a fractional test meal which showed the presence of starch throughout. (Fig. 1.) In addition, the meal showed a very high acid curve, both free and combined. Three weeks after the operation the vomiting from the pyloric stenosis became less marked and eventually subsided. The patient began to feel much better, enjoyed his small meals and began to put on weight. He was discharged in fairly good condition after six weeks in the hospital.

COMMENTS

According to the barium meal report on October 24, 1950, there had been considerable irregularity and deformity of the duodenal cap due to chronic ulceration. A repeated barium meal test on November 28, 1950 showed the ulcer niche to be small but still present. There was a considerable amount of contraction but the stomach emptied normally. (It is to be noted that in these barium meal tests in 1950, only the duodenal ulcer was present. This suggests that the gastric ulcer found perforated at the operation was secondary to the duodenal ulcer.)

Acknowledgment: I wish to express my thanks to Mr. T. Henry Wilson for allowing me to publish this case, and to Mr. Norman Tanner for his advice and encouragement to do so.

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Surgery Court Cases

HOWARD NEWCOMB MORSE,* *Chicago, Illinois*

BEADLES VS. METAYKA

Supreme Court of Colorado

311 P. 2d 711

This was an action for damages by a patient against a surgeon for personal injuries sustained by the patient when he fell off an operating table in the hospital after he had been rendered unconscious by an anesthetic. The District Court of El Paso County, Colorado, rendered judgment for the patient, and the surgeon appealed.

When the accident occurred, the unconscious patient was on his back on the operating table, and the anesthetist was engaged in checking and recording respiration, pulse and other related matters concerning the condition of the patient. An orderly was at the foot of the operating table and the anesthetist was at the patient's head.

The surgeon entered the room and, although not being fully gowned and requiring a nurse to tie his gown, gave orders to place the patient on his side, which the orderly proceeded to do. The orderly was holding the patient by the hips in the position as directed when he was then told to "get a strap" or "strap the patient." The surgeon turned to have his gown tied, and the anesthetist turned her head and began making entries on the chart. The orderly left the side of the operating table to get the strap as directed. The patient then fell to the floor and was injured.

The Supreme Court of Colorado, in affirming the decision of the lower court, declared that the surgeon "had entered the operating room and had assumed command and responsibility by giving direct orders concerning the placing of the patient in position on the operating table, even though he was not actually at the side of the patient at that moment ready to make the first incision . . . it was negligence on the part of the surgeon to order the attendant to do anything which might take him away from the physical person of the patient without first assuring that someone was at hand to attend and hold the patient."

SCARANO VS. SCHNOOR

District Court of Appeal of California

323 P. 2d 178

This was an action against a surgeon for alleged negligence in performing an operation on the eye. The Superior Court of Alameda County, California, entered judgment for the surgeon, and the patient, through her guardian *ad litem*, appealed.

The surgeon's diagnosis was that the patient, a seven and a half year old girl, had a congenital bilateral displacement condition with cataractous changes (opacity of the lenses). He recommended surgery as the only method of correcting her vision. Surgery was advised at this time because vision develops until approximately eight years of age and to improve vision the surgery must take place before that time.

The patient's left eye was operated upon. The operating procedure employed was that of the intracapsular extraction. This method consists of the removal of the entire lens in-

* Counsellor at Law of the Supreme Court of the United States of America.

cluding the capsule (which contains the lens substance). The lens is held in place by zonular fibers and in removing the lens these fibers must be broken. When there is a displaced lens in a child, the fibers are usually stretched on one side and very strong on the opposite side. The surgeon testified that while he had expected this condition the zonular fibers proved tougher than he had anticipated. He was unable to break these strong fibers by pulling or twisting the lens and had to use a loop. This instrument is placed under the lens to give greater traction.

The vision in the patient's left eye was 20/40 to 20/50, which was an improvement from that prior to surgery. Due to a "hammocking" of the pupil (the iris drawing up and closing the pupil) a visual iridectomy was performed by the surgeon. This operation consists of cutting a hole in the iris to permit vision.

The patient's vision did not improve and she was taken to another surgeon (not the defendant). The second surgeon found marked inflammation in the eye with poor light perception. He also found early signs of phthisis bulbi, or shrinking of the eyeball. These conditions were due to a loss of the vitreous substance of the eye. It was finally decided that the eye would not improve and it was removed and a prosthesis installed.

The lower court had instructed the jury that if the evidence in the case left it just as probable that the injury was the result of one cause as much as another, the patient could not recover. The attorney for the patient's guardian *ad litem* argued that this instruction was improper on the basis that it would be understood by the jury to mean that if they found that the injury proximately resulted from both causes, one of which would render the surgeon liable, they must nevertheless decide in favor of the surgeon. The District Court of Appeal of California rejected this contention and affirmed the decision of the trial court.

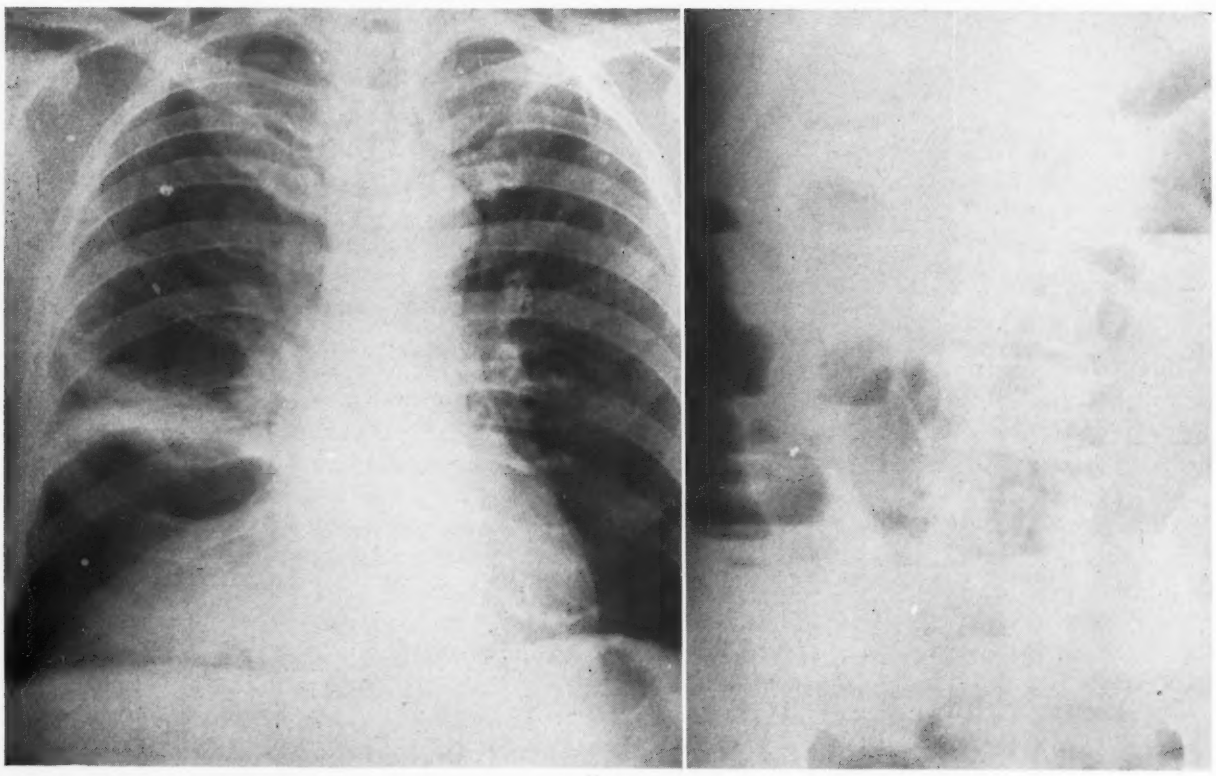
The District Court of Appeal stated: ". . . the negligence of the defendant (the surgeon) need not be the sole proximate cause and . . . the defendant is liable where his negligence is *one of several* contributing factors, each of which is a proximate cause . . . to recover plaintiff must prove that the injury was wholly or *partly* the result of that cause which would render the defendant liable."

The Diagnostic Corner

A CLINICAL and radiologic teaching exercise pertaining to a complication seen following conservative management of an acute surgical condition within the abdomen.

SIDNEY W. NELSON, M.D., *Columbus, Ohio*

From the Department of Radiology, The Ohio State University Health Center, Columbus, Obio.



The Diagnostic Corner

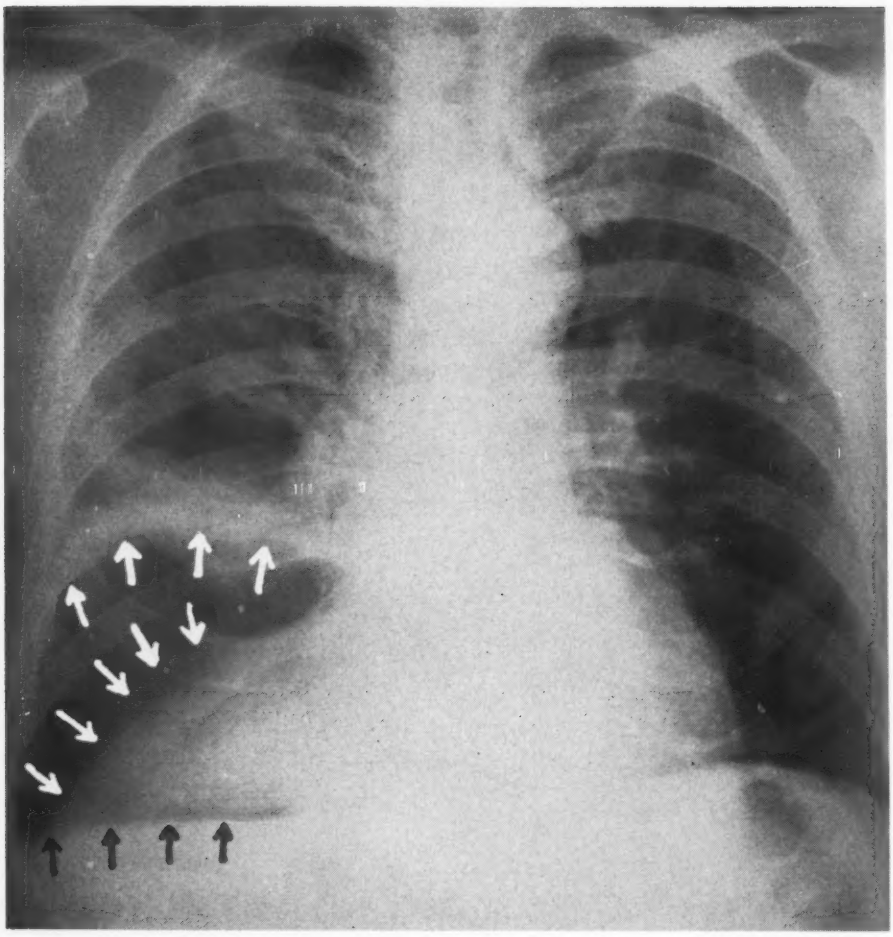
SEVEN weeks prior to admission to the Ohio State University Hospital this fifty-seven year old white man had been admitted to another institution because of a sudden onset of severe upper abdominal pain. Although it was suspected that the patient had a perforated peptic ulcer, conservative management was considered the best treatment and was thus started. One week after the illness began, the patient was believed to have had a myocardial infarction, for which he was treated. The abdominal pain failed to diminish and generalized progressive weakness ensued. The gradual deterioration in the patient's condition resulted in his being admitted to the Ohio State University Hospital, at which time physical examination showed a well developed, well nourished white man in moderate distress due to a markedly distended abdomen and generalized weakness. The abdomen was doughy to palpation and there was tenderness to palpation in the right upper quadrant. No masses could be palpated and the bowel sounds were present. The patient was sent to the radiology department where films were obtained of the chest and abdomen. The upright films of the chest and abdomen clearly demonstrate the findings which might be expected in a patient with this history.

What is your diagnosis?

Please turn page for answer

Diagnosis

Huge right subphrenic abscess secondary to perforated peptic ulcer (gastric).



The history of a sudden onset of severe upper abdominal pain seven weeks earlier, followed by persistent abdominal pain and increasing abdominal distention and generalized weakness, should certainly suggest the diagnosis of a perforated peptic ulcer and subsequent peritonitis. The upright regular chest x-ray film clearly shows a huge abscess below the markedly elevated right hemidiaphragm. The normally sharp outline of the superior margin of the right hemidiaphragm is obscured by the pneumonia and small amount of pleural fluid in the right costophrenic angle, these latter findings frequently being associated with a subphrenic abscess. There is a large amount of free gas between the elevated right hemidiaphragm (upper row of white arrows) and the dome of the liver (lower row of white arrows), which is seen projected above the large fluid level (black arrows) in the inferior portion of the large abscess cavity.

The upright abdominal film shows multiple small air-fluid levels in the right side of the abdomen, typical of the type of small bowel and colon stasis due to paralytic ileus. The most common cause of paralytic ileus is peritonitis, the paralytic ileus in the case herein described being due to the persistent low grade inflammatory effect on those segments of small bowel and colon adjacent to the walled-off huge right subphrenic abscess. The rather gray appearance of the abdominal film is due to the fluid and exudate within the peritoneal cavity outside the main abscess.

Incision and drainage of the abscess was performed under general anesthesia using the posterior approach. A de Pezzer catheter was left in the abscess cavity which was irrigated daily. Vigorous antibiotic therapy was given throughout the postsurgical period. The patient made slow but progressive improvement and the catheter was removed three days prior to discharge, at which time the patient had been afebrile for fifteen days.

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Case Analysis Clinic

The management of an acute abdominal emergency complicated by hematologic disease and steroid therapy.

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From the Department of Surgery, The Ohio State University School of Medicine, Columbus, Ohio.

THE patient, a fifty-six year old man, was admitted to the hospital at 9 P.M., eighteen hours after the onset of acute abdominal pain. He had been treated on the Hematology Service for proved Hodgkin's disease with a variety of therapeutic agents, and results were satisfactory. For several months before this admission he was treated with chlorambucil and prednisone. The latter, an adrenocorticosteroid, was given in a dosage of 15 mg. daily. On this regimen his general condition was fairly good. For several weeks before the acute episode, however, he had noted vague "indigestion" with postprandial fullness and eructation, but there was no pain of any sort. He also was constipated for several weeks. He used alka-seltzer to relieve the symptoms. After an uneventful day the patient woke at 3 A.M. of the day of admission with severe abdominal pain first noted in both lower quadrants. The pain came on suddenly. It was severe, continuous, steady, sharp and unremitting; it did not radiate. There was mild shoulder pain bilaterally, made worse by motion and deep inspiration, but not accompanied by nausea, vomiting or the desire to urinate or defecate. It was totally different from anything the patient had previously experienced. He finally obtained partial relief when a physician administered a narcotic. He then sent the patient to the hospital.

PHYSICAL AND LABORATORY FINDINGS

The patient was poorly nourished; he appeared both chronically and acutely ill and complained of severe abdominal pain especially in both lower quadrants. Temperature was 99.6°F., pulse 124, blood pressure 92/62 mm. Hg, respirations 32 per minute, shallow and almost entirely thoracic. Skin turgor was poor, and the mucosae and nail beds were quite pale. Large, hard lymph nodes were palpable in the neck and axillas.

The chest was clear and heart sounds were normal. The abdomen was slightly distended with definite but not board-like over-all rigidity. There was generalized abdominal tenderness, with rebound tenderness more marked in the lower quadrants and especially in the right lower quadrant. With the limitations of tenderness and rigidity, no organs or masses were palpated. On auscultation the abdomen was silent. There was exaggeration of pain on movement, coughing or deep inspiration. Liver dullness was present on percussion. Examination of the rectum disclosed fullness and some tenderness in the cul-de-sac. Feces was normal in color although positive upon testing with guaiac for occult blood.

Laboratory examinations included a peripheral hemogram; hematocrit was 30 per cent, hemoglobin 8.2 gm. per cent, white cell count 1,700 per cu. mm. with 30 non-segmented forms, 50 segmented, 15 lymphocytes, 0 esosinophils, 0 basophils and 5 monocytes. Urine obtained by catheter was scant, hazy amber in color and had a specific gravity of 1.030. It was otherwise normal. Serum amylase was 220 units, blood urea nitrogen 34 mg., prothrombin 60 per cent of normal, serum sodium 147 mEq., potassium 3.4 mEq., chloride 100 mEq., CO_2 combining power 76 vol. per cent. At the same time blood was drawn for typing and crossmatching. A generous supply of whole blood was ordered. An intravenous infusion of 5 per cent dextrose in physiologic saline solution was started. A Levin tube was passed, gastric suction was started and parenteral chloramphenicol was administered. The patient was sent to the Department of Radiology for chest films, flat and upright films of the abdomen and a left lateral decubitus film of the abdomen.

DIFFERENTIAL DIAGNOSIS

The history of severe, steady abdominal pain of sudden onset, with evident signs of generalized peritonitis, dehydration and hypovolemia, strongly suggested acute, free perforation of the gastrointestinal tract.

The role of the underlying Hodgkin's disease and the medications exhibited must be evaluated. The relationship of the corticosteroids to ulcerogenesis has been frequently indicated. These agents induce a marked gastric hypersecretion. They apparently affect at least total volume and acidity. It may well be that they likewise interfere with the healing process which occurs simultaneously with gastroduodenal ulceration. The occurrence, therefore, of gastroduodenal ulceration and perforation in patients on prolonged corticosteroid therapy is not uncommon. It must always be placed high on the list of differential diagnoses in the patient with an acute surgical condition of the abdomen who has received steroids. In this particular patient, however, the distribution of pain was not typical for gastroduodenal perforation. In such perforations onset in the upper abdomen is usual. Then it spreads down the right paracolic gutter as the highly irritant gastric juice drains along this route. Later it involves the whole abdomen, but the signs usually are maximal in the upper quadrants. Onset in the lower abdomen, with maximal signs in the lower quadrants, is feasible but atypical. This, together with an irregular bowel history prior to the acute episode, raises the possibility of perforation of the colon due to carcinoma or diverticulitis. It is interesting to speculate that corticoid therapy might interfere with the localization of a perforated diverticulitis.

With the tentative diagnosis of perforation of the gastrointestinal tract, it is routine to begin gastric suction to minimize further soliage and because of the adynamic ileus secondary to peritonitis. The general problems are to treat dehydration and shock, minimize further peritoneal contamination and control infection. Antibiotics should therefore be used promptly since infection will be a critical component of the problem no matter where the perforation has occurred. Even aside from physical signs indicating dehydration and hypovolemia with oliguria and azotemia (blood urea nitrogen 34 mg.), the presence of peritonitis *per se* indicates a deficit of extracellular fluid and electrolytes as well as colloid and whole blood. This is similar in mechanism, amount and type to that resulting from an extensive burn. It was clear that the patient required replacement therapy; this should include water, electrolytes, colloid and whole blood. The first fluid started when an extracellular fluid deficit is diagnosed should be isotonic saline solution. Serum albumin or stored plasma may be administered at the same time, particularly when signs of shock are apparent. Blood is administered when typing and crossmatching are complete and blood is available.

The electrolyte pattern disclosed by the laboratory was compatible with the history of steroid therapy. There was some elevation of serum sodium and a decrease in serum potassium concentrations characteristic of the known sodium retention and potassium loss produced by corticoids. Potassium was not administered parenterally until satisfactory urinary output was shown.

The peripheral hemogram with severe anemia and leukopenia reflected the underlying hemotologic disease, and its treatment with chlorambucil and similar agents.

Radiologic examination disclosed gas under both hemidiaphragms in an otherwise normal chest film. The supine, lateral decubitus and upright films of the abdomen showed evidence of paralytic ileus with moderate amounts of gas throughout the small intestine and colon, and free gas beneath the diaphragm and lateral to the liver.

A perforation therefore was confirmed. Certainly a gastroduodenal site seemed most likely, but the atypical manifestations still left room for uncertainty. Needle paracentesis was performed after radiologic examination. A 20 gauge spinal needle was inserted into the right lower quadrant. Abundant fluid was found and sampled. The fluid was yellow, turbid and odorless. It contained many leukocytes, a few bacteria (cocci), bile and had an amylase content of 660 units. This left no question about the gastroduodenal site of perforation. In the presence of colonic perforation one expects many bacteria with abundant rods, detritus, no bile and an amylase value no higher than that of the serum. A fecal odor is also expected.

TREATMENT

With the diagnosis clear it was necessary to decide whether this perforation was to be

surgically closed. In this very poor risk patient it was tempting to consider non-operative treatment. This would include nasogastric suction, fluid and blood replacement, and massive antibiotic therapy. Results comparable with surgical closure have been claimed for this method. In this instance, however, it was believed that the history of steroid therapy would make sealing of the perforation less likely. It has been shown that the adrenal corticoids interfere with the inflammatory process and the sealing of such lesions. It was therefore decided that surgical closure was the safer course.

In preparation for surgery the patient was given intravenously 2,000 ml. of electrolyte solution containing 100 mg. of hydrocortisone and 1,000 ml. of whole blood. He was taken to the operating room six hours after admission with a third 500 ml. unit of blood running. Blood pressure at that time was 118/82 mm. Hg, pulse 104, temperature 100°F.; the urinary output was above 35 ml. per hour. Since prolonged steroid therapy leads to adrenal atrophy and poor response to stress, the intravenous hydrocortisone was deemed an important preoperative measure. In this era when therapeutic use of corticosteroids is common, this factor must not be overlooked. Such a patient, if not provided with exogenous hormone, will in essence behave like a patient with Addison's disease. He will respond badly to surgical stress.

With the patient under general anesthesia the abdomen was entered through a short upper midline incision. Large amounts of free fluid and air were found. This was aspirated as completely as possible. A free perforation about 7 mm. in diameter was found on the anterior wall of the gastric antrum. There was no evidence of any sealing-off process and there was very little reaction around the lesion. Peritoneal fluid was sent to the laboratory for bacteriologic and antibiotic sensitivity studies. This is an important part of any such surgery because of the importance of control of infection. The lesion was excised for tissue examination and to permit better closure. Simple suture closure was performed and the area was covered with an omental flap. A solution of 500 mg. of Neomycin in 150 ml. of saline was instilled in various areas of the peritoneal cavity. A Stamm gastrostomy was made, using a No. 18 Robinson catheter, and the abdomen was closed. In the patient in whom prolonged gastric suction is anticipated, gastrostomy has been a boon. It permits patient comfort, efficient aspiration and minimizes respiratory complications.

POSTOPERATIVE COURSE

Postoperatively the care was, for the most part, routine. Gastric suction was maintained by way of the gastrostomy tube. Antibiotic therapy was adjusted according to the sensitivities determined from the peritoneal fluid which grew streptococci, coliform organisms and proteus. Administration of steroid was continued. This was still an important component of the care because of the adrenal atrophy already mentioned. In the usual case the hormone is slowly withdrawn by gradually reducing the daily dose over a period of about a week, and concomitantly giving ACTH for a few days. This stimulates adrenal growth and activity and prepares the glands to assume their normal burden. The hematologist believed that in this patient indefinite steroid therapy was necessary for the hematologic disease. No attempt to reduce the dosage was therefore made.

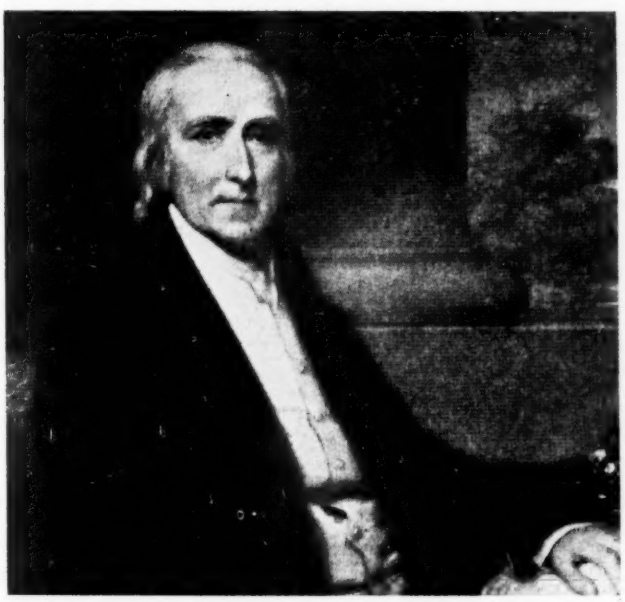
Tissue examination showed only perforated benign gastric ulcer.

The patient's convalescence was remarkably smooth and he was discharged on the sixteenth postoperative day. He was taking the original dose of 15 mg. of prednisone daily but was on a rigid ulcer-type diet reinforced by antacids and an anticholinergic drug. It would seem desirable that all patients on prolonged conticosteroid medication should observe such precautions in order to minimize gastroduodenal ulceration.

Our Surgical Heritage

D. P. HALL, M.D., *Surgical Department, University of Louisville, Louisville, Kentucky*

UNITED STATES OF AMERICA



PHILIP SYNG PHYSICK

PHILIP Syng Physick was born in Philadelphia on July 7, 1768. His father was a man of affluence and was Keeper of the Great Seal of the Colony of Pennsylvania before the American Revolution. It is said that Physick received much of his piety and fondness for educational pursuits from his mother. During 1800 Philip Syng Physick married Elizabeth Emlen, the talented daughter of a minister of the Society of Friends. Two sons and two daughters were born.

Physick received his basic education in an academy maintained by the Society of Friends, after which he matriculated in the University of Pennsylvania and received the Bachelor of Arts degree in May, 1785. The father of Philip Syng Physick took the youth to London where the advantages of a medical education were superior to those in the United States. He became a private pupil of John Hunter in January, 1789, and received an appointment as House Officer at St. George's Hospital in London, due to the influence of John Hunter. In January, 1791, Physick completed his residency at St. George's Hospital, after which he was elected a Fellow of the

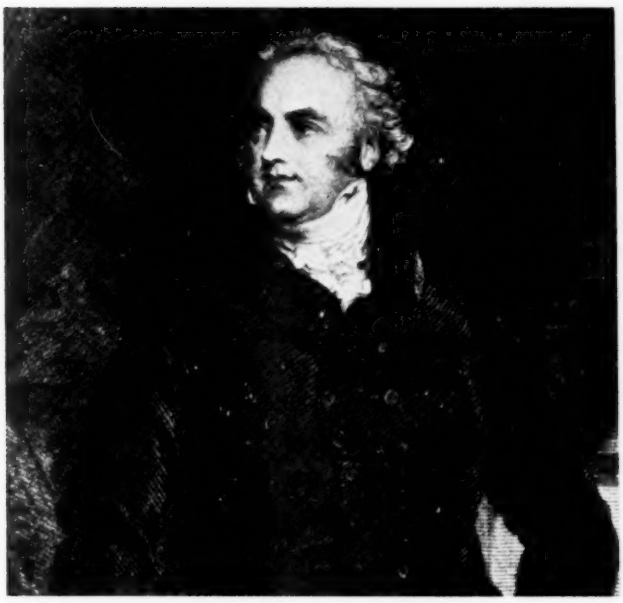
Royal College of Surgeons of England. The University of Edinburgh was in high favor with American medical students. It was only natural that Physick matriculated at the University of Edinburgh and received training at the Royal Infirmary; he graduated with the degree of M.D. in May, 1792. At this time he made a rather significant contribution to surgery on the causes of intussusception of the small bowel into the colon.

Physick returned to Philadelphia and established himself in practice in September, 1792, and, as Gross writes, "For several years he trod the alleys and byways of his native city before his income was sufficient to pay for his shoestrings." In 1805 a separate chair of surgery was established by the University of Pennsylvania. Philip Syng Physick became Professor of Surgery in this institution.

Physick was one of the first to advocate immediate closure of puncture wounds of the chest. He described diverticula of the rectum and in January, 1826, he successfully performed an original operation for artificial anus. The most valuable contribution of Physick to surgery other than his teaching was the introduction of animal tissue for ligature.

Philip Syng Physick died on December 15, 1837, from myocardial failure and thus the first great American surgeon passed away.

EUROPE



SIR ASTLEY PASTON COOPER

Sir Astley Paston Cooper, the son of a clergyman and grandson of a surgeon, was born in Brooke, England, in 1768. He studied medicine at Edinburgh and then at London as a student of John Hunter, he of the "don't think, but try" teaching.

In 1789 Cooper was made demonstrator of anatomy at Saint Thomas Hospital and in 1800 surgeon to Guy's Hospital. He worked hard and incessantly. He performed dissections every day of his life; when traveling he paid large fees to body snatchers for material.

His daily routine was to rise at six o'clock, dissect until eight o'clock, breakfast on two rolls and tea, see charity patients until nine o'clock, attend his consulting practice until one o'clock, then visit the wards of Guy's Hospital and operate upon private patients until seven o'clock.

Cooper was one of the world's great surgical technicians. It was said he could operate easily with an oyster knife.

Astley Cooper was the surgical mentor to more American surgeons than any one of his time. He was a pioneer in vascular surgery and an exponent of experimental surgery.

Cooper's contributions to surgery have been lasting; all know Cooper's ligament and Cooper's hernia (retroperitoneal). In 1817 he ligated the abdominal aorta and in 1808 successfully ligated the common carotid artery. His books were of the highest order: "Hernia," 1804; "Injuries of the Joints," 1822; "Diseases of the Breast," 1829; "Diseases of the Testes," 1830; and "The Anatomy of the Thymus Gland," 1832.

Sir Astley Paston Cooper died in 1841 as the most popular surgeon in the public eye, a prodigious worker and the revered teacher to a host of American surgeons. His life was not "an act of common passage, but a strain of rareness."

Book Reviews

The Acute Abdomen. By William Requarth, M.D. Second edition, 313 pages. The Year Book Publishers, Inc. Chicago, 1958. *Price* $6.50.

This is the second edition of this book previously published under the title "Diagnosis of Acute Abdominal Pain." With the change in title, the author conforms more closely to his subject matter.

The entire monograph is excellently written. The author's groupings of subjects are different and much more practical than commonly found. After the initial chapters on examination and differential diagnosis from the standpoint of location and type of pain, he presents an excellent section on intestinal obstruction. This provides, especially for the student, a workable approach to this problem and includes detailed management.

Following this the author discusses the conditions requiring immediate operation, delayed operation and conditions in which operations are contraindicated or harmful. These three sections are well thought out and clearly presented. He then closes with sections regarding traumatic wounds of the abdomen, diagnosis of acute abdominal conditions in infants and the differential diagnosis of acute gastroesophageal hemorrhage.

The book is written in a broad sense so that the beginning student will be able to follow, and yet some of the diagnostic points are very worthwhile for the practicing surgeon. It should be *must* reading for all students, house officers and young practicing physicians, not just surgeons.

RICHARD J. IRETON, M.D.

General Diagnosis and Therapy of Skin Diseases. By Hermann Werner Siemens, M.D. Translated from the German Edition by Kurt Wiener, M.D. 311 pages, 375 illustrations. The University of Chicago Press. Chicago, 1958. *Price* $10.00.

This is a book which was apparently written for use in teaching dermatology to medical students and is not one which either general practitioners or internists other than dermatologists would be likely to consult. It is quite typical of European literature in that it is very detailed and in some areas it is difficult to find a specific treatment for a given dermatological disorder.

The book is divided into two parts. One is devoted to general diagnosis and the other to general principles of therapy. In the second part the author deals almost entirely with local therapy.

In summary, this book can be considered a good reference primarily for dermatologists.

R. D. WILLIAMS, M.D.

The Physiology and Pathology of the Cerebellum. Edited by Robert S. Dow, M.D., PH.D. and Guiseppe Moruzzi, M.D. 675 pages, 185 illustrations. The University of Minnesota Press. Minneapolis, 1958. *Price* $12.50.

The text is an authoritative volume dealing with the physiology and pathology of the cerebellum. The authors present an exhaustive and comprehensive review of all the experimental work on the cerebellum. This includes previous and recent ablative and stimulative work on the cerebellum of lower animal forms, submammals and mammals.

Cerebellar relations to other central structures such as the spinal, labyrinthine, vestibular and vegetative systems, as well as the cerebral cortex, are given in detail. A thorough and interesting section dealing with the electrophysiology of the cerebellum is presented. This is followed by excellent sections on cerebellar functions and clinical symptomatology of cerebellar disorders.

Extracerebellar lesions simulating cerebellar lesions are discussed. Following in succession are sections dealing with hyperkinetic disorders, developmental anomalies, atrophic lesions, acute inflammatory and toxic dis-

orders, infectious lesions, vascular lesions, trauma and tumors of the cerebellum.

The entire volume is an authoritative compilation of cerebellar physiology and pathology, and will be found to be an extremely valuable source of reference for the experimental neurophysiologist and the clinician.

J. N. MEAGHER, M.D.

Surgery in Infancy and Childhood. By Matthew White, M.A., M.B., CH.B., F.R.F.P.S. (Glas.), F.R.C.S. (Edin.) and Wallace M. Dennison, M.D., F.R.F.P.S. (Glas.), F.R.C.S. (Edin.), F.I.C.S. 444 pages. E. & S. Livingstone, Ltd. Edinburgh, 1958. *Price* $9.50.

This well printed and illustrated book nicely accomplishes its purpose of introducing in a brief and succinct fashion the surgical problems of infancy and childhood. This book is primarily designed for medical students and for physicians who are not primarily engaged in practice in this field. The book covers a very wide range of topics, including pre- and postoperative care, anesthesia, trauma, infection, diseases of the gastrointestinal tract, genitourinary disorders, surgical problems in the thorax, surgical problems of the head, and disorders of the musculoskeletal system.

It is apparent that a book with such a wide range can only briefly summarize the important points of any single topic. The first four chapters of the book properly emphasize the differences between children and adults, pre- and postoperative care, anesthesia, trauma and infection. Much of the basic information essential to an understanding of the surgical problems of infancy and childhood is included in these topics.

In most of the remaining chapters the surgical problems peculiar to a particular anatomic area are presented. For the most part these subjects are dealt with quite briefly, with only the most significant points concerning the clinical features and the necessary treatment being presented. The more important surgical problems of this age group, such as tracheoesophageal fistula, intussusception, appendicitis and hypertrophic pyloric stenosis are given a considerably more complete discussion. The very excellent drawings and photographs, some of them in color, add greatly to the clarity and usefulness of the text.

E. THOMAS BOLES, JR., M.D.

Atomic Energy in Medicine. By K. E. Halnan, M.D., D.M.R.T. 157 pages. Philosophical Library, Inc. New York, 1958. *Price* $6.00.

Dr. Halnan summarizes recent advances in a potentially complicated and broad subject to the reader who has little knowledge of medicine or physics.

The eleven chapters of this book include general discussions of the concept of nuclear physics, the characteristics of radioactive isotopes, the applications of these substances to medical research, the biological effects of radiation, methods currently used in cancer therapy, radioactive iodine and thyroid disease, the use of isotopes in blood dyscrasias, general applications of radioactivity to specific medical and surgical problems, the use of high energy particle accelerators, radiation hazards and possible future uses of radioactive isotopes.

This book is well presented and achieves the author's aim as a general introduction to a new and progressing field in medicine.

CLARENCE I. BRITT, M.D.

Emergency War Surgery, NATO Handbook. U. S. Government Printing Office. Washington, D. C., 1958. *Price* $2.25.

This handbook represents the choice combination of material obtained from publications of the NATO nations. Few textbooks contain such a modern approach. None can be obtained at less expense.

This is a handbook; it is not a military manual in the usual sense. Policies or regulations for the care of the wounded are specifically outlined. Those principles of initial and follow through care which have been learned from experiences with civilian and war injuries in many countries are presented in an easily understood manner.

The text is divided into four sections: The first three are of almost as much value in civilian surgery of trauma as in war surgery. The review of various types of wounds and injuries in Part I is clear, concise and worth review by all physicians. The discussions in Part II of shock, metabolic disturbances and infection as the responses to trauma are excellent and clearly define the rationale of treatment. Part III deals with general principles in the management of many injuries and Part IV defines regional wound care.

Much of the material outlined in this book is unfortunately lacking from the usual textbook of surgery. It would take an exhaustive amount of reading to gain similar information which has been given concisely in this handbook. Although designed primarily for use by physicians of NATO armed services, it is to be highly recommended for students and resident surgeons.

ROGER D. WILLIAMS, M.D.

Pathophysiology in Surgery. James D. Hardy, M.S. (Chem.), M.D., F.A.C.S. 704 pages. Williams and Wilkins Co. Baltimore, Md. *Price* $19.00.

This is a new type of book written in its entirety by one author. It is easily readable, consistent and extensively illustrated. It emphasizes the application and correlation of total body physiology on the patient care level. Numerous brief case summaries are presented to lend clarity to the points being discussed. The book is well organized and adequately indexed. In its chapters are found a digest of the best of recent surgical literature and research. These are correlated and combined with the experience and concepts of the author.

The first ten chapters deal with general body physiology that directly concerns the practicing surgeon. They are rich in the modern concepts of such subjects as injury, nutrition, healing, homotransplants and radioisotopes. The remaining eleven chapters cover the body organ systems. These chapters are concerned with a brief review of normal physiology, then an understanding of pathophysiological principles. Problems of therapy and management are also considered. Each chapter is followed by a list of worthwhile and pertinent references.

This book is a must for residents in surgery. It will also be found extremely informative and useful by graduate surgeons. Although not a text in general surgery, it should be of great interest to the medical student who is interested in a career in surgery.

HENRY KELLEY, M.D.

The Essence of Surgery. By C. Stuart Welch, M.S., M.D., PH.D. and Samuel R. Powers, Jr., A.B., M.D., M.SC.D. W. B. Saunders Company. Philadelphia, 1958.

This book is designed as an introduction to surgery. It presents the field of surgery and the surgeon in clear, concise terms. The authors hold that surgery is basically concerned with the management of acute injury (not necessarily trauma but rather any action detrimental to the human body). They further believe that surgery can be divided into four types: treatment of wounds, extirpative surgery, reconstructive surgery and physiologic surgery.

The book begins with a short history of surgery. Then there are two excellent sections on body injury and loss of body tissues. The latter section is well written. There are sections on loss of body fluids, infection, and pre- and postoperative care.

There is a nice section on surgical technic which the authors believe is frequently neglected, and three main sections on extirpative, reconstructive and physiologic surgery. These present their points well and are nicely written. The book closes with a brief section on anesthesia.

I believe every surgeon should read this book and that it will be invaluable in student teaching at an early, introductory level.

RICHARD J. IRETON, M.D.

Medical Electrical Equipment. Advisory Editor, Robert E. Molloy, M.B., F.F.A., R.C.S. 238 illustrations, 312 pages. Philosophical Library, Inc. New York, 1958. *Price* $15.00.

This book contains a great deal of information on a wide range of electrical devices in general hospital use. The equipment described here is of British make, but the notes on maintenance and operation can be applied to the American equivalents. This is a useful book for operating room, central supply and maintenance personnel.

HOWARD D. SIRAK, M.D.

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